LEAD ABSORPTION AND THE HEALTH OF A COMMUNITY.

Studies arising from the lead solvent properties of Innerleithen Water Supply.

A thesis presented for the degree of Doctor of Medicine

by

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PREFACE

One part of the work of the general practitioner is the presentation of unsolved clinical problems to consultants in different subjects. By an extension of this normal practice, the problems to be described have been placed before specialists in many different scientific fields. Their response in patient guidance and helpfulness has far exceeded any reasonable expectation and has made these studies possible. It has been a great privilege to receive their help and it is as great a pleasure to acknowledge it.

Innerleithen 1965.

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SECTION I

General Introduction

Plate 1.

Normal appearance of Innerleithen water in the absence of heavy rainfall. (5/9/64)

Plate 2.

Marked discolouration of Innerleithen water after 1.2 inches of rain in 48 hours. (19/8/64).

Facing page 1.

Introduction.

After heavy rain the water supplies of our small town showed a marked discolouration which was quite obvious to the naked eye. This provided the original problem from which these studies began and is demonstrated by the comparison of Plates 1 and 2. It is not difficult to appreciate how anyone unaccustomed to this might wonder if water having such an unpleasant appearance could have harmful effects on the consumers.

Within a few months of my arrival in this town in 1958, my patients began complaining to me of a recurring gastro-enteritis which they associated with the water supplies. The first two complainants were businessmen who had a wide range of contacts in the area. Both had children suffering from this ailment at the time. There was no connection between them, but neither was a native of the town and both commented on the frequency with which their families were upset and on how often they encountered this illness in the course of their dealings with the public. This was quite different from their previous experience elsewhere.

Another complainant was much more specific in her comment. She said "When the Tweed is in spate, the water goes brown, the tea tastes awful and we all get diarrhoea". Since tea is made with boiling water this suggested the possibility of a chemical cause rather than a bacteriological one.

Discussion of this with the Burgh Surveyor - the official responsible for the water supply - revealed that he also had had complaints. To use his phrase, it seemed as if the water was acting "like a dose of salts", but his repeated water analyses, both bacteriological and chemical, showed nothing to account for this. Subsequent analyses were also reported as satisfactory both from routine sampling and from special samples taken after outbreaks of

this type of gastro-enteritis.

This impasse persisted for two years. The assurances of the analyst that the water supplies contained no toxic or irritant material were accepted somewhat reluctantly in view of the very obvious alterations in the character of the water.

Some patients with this affliction commented that even their dog had diarrhoea. No foodstuff common to man and animal could be found suspect. I was impressed by this point partly because on a number of occasions I was roused from my bed by the demands of my own dog to be let out. The diarrhoea of the doctor's dog seemed to herald the onset of a fresh wave of gastro-enteritis cases.

The gastro-enteritis was regarded as a form of food poisoning and attempts were made to trace its source. In winter, outlying parts of the practice offer considerable advantages for epidemiological studies, as they have little contact with the rest of the community. Despite this it proved impossible to trace a source of infection in such cases. Culture of stool samples from patients with gastro-enteritis was also completely unhelpful.

An enquiry to a different water analyst about the possible presence of chemicals which might act like "a dose of salts" only produced confirmation that there was no excess of sulphates in the water supplies in the area.

An observation which was not at the time related to gastro-enteritis was made in a general discussion on haematology by the pathologist to the Border Hospitals Group. He mentioned that he had on a few occasions observed punctate basophilia in the course of routine blood examinations. These were from various parts of the wide area covered by his laboratory and no cause had been discovered for them.

A direct question was later put to yet another analyst on whether any intermittent chemical contamination was possible which might escape detection by routine analysis, but be capable of causing gastro-intestinal disturbance. This analyst immediately commented on the aggressive potentialities of moorland surface water, that is, their tendency to attack lead and copper piping.

Water samples were sent to him for examination for lead content. These were taken specifically for that purpose from the first running of the taps in the morning. On a number of occasions lead was found in excess of the World Health Organisation International Standard Limit for lead content of drinking water.

In this way, the interest in the intermittent discolouration of the water supplies and in the endemic gastro-enteritis in the area gave rise to the discovery that the water supplies were able to dissolve lead from lead water pipes. Though gastro-intestinal disturbances are a well known feature of lead intoxication, the discovery of abnormal amounts of lead in the water supply by no means proved that this was causing acute gastro-enteritis.

This finding did, however, become the starting point for a number of other studies. An attempt was made to assess the worst concentration of lead in the water to which patients in the practice might be exposed. Evidence was obtained of an association between the plumbo-solvency of the water and the disturbance in the water supply produced by heavy rainfall.

Patients suffering from gastro-enteritis were investigated for evidence of increased lead absorption by examination of blood films for punctate basophilia and by blood lead estimation.

The maternity patients in the practice were exposed to an abnormal intake of lead from these water

supplies. Bell, Hendry and Annett (1925) claimed that lead had a selective affinity for the chorionic epithelium without the maternal organism being in any way affected. An industrial screening test for increased urine coproporphyrin excretion was therefore added to the routine of antenatal care in an attempt to discover early signs of lead toxicity.

The use of this coproporphyrin test and of examination of blood films for punctate basophilia, made it possible also to screen a large number of patients suffering from a wide variety of other conditions for evidence of increased absorption of lead.

The absorption of lead is dependent not only on the intake of lead in water, but also on the amount of lead present in the food. Studies were therefore made of the lead content of food and especially of milk in the practice, since the cows in byres in winter were also supplied with lead-piped water.

These studies have extended over a period of six years. The order in which they were carried out has depended on the availability of advice and especially on the provision of facilities. These facilities have frequently been of a type not usually available to a general practitioner and have been granted by special arrangement. I am extremely grateful for these. It should be realised, however, that at times these were not available or were very restricted. These factors coupled with the seasonal fluctuations in the normal work of a general practitioner, have prevented the whole sequence of studies from being conducted according to a preconceived co-ordinated research programme. Thus the final step was the analysis for lead content of a complete two day diet for one of the patients. It was only after this was completed that it was possible to view the pattern of lead absorption in this practice in proper perspective.

Rather than adhere to the order in which these investigations were carried out, it will be more suitable to present the details of the various sources of lead prior to the clinical observations of the resulting effects. Some reference must first be made to parts of the extensive history of lead poisoning which are relevant and to the methods of study which are available.

The History of Lead Poisoning.

The poisonous effects of lead were well recognised in ancient times. Nikander (175-135 B.C.) described acute lead poisoning with astringent effects on the mouth and throat, flatulence and abdominal distension, dizziness, stupor and death. Paulus Aegineta (629-690 A.D.) referred to disorder of the intellect and difficulty of moving, and also to heaviness of the stomach and bowels with intense pain, sometimes wounding the intestines, and causing retention of urine and swelling of the body (Trans. Adams 1846). His description of an epidemic of colic terminating in paralysis, according to Major (1955), is the earliest known description of the clinical picture of lead colic, but Hunter (1957) notes that Hippocrates (370 B.C.) described a severe attack of colic in a man who extracted metals and was probably the first of the ancients to recognise lead as the cause of the symptoms.

Pliny (A.D. 23-79) gave a description of lead workers protecting their faces with masks of loose bladder-skin to avoid inhaling the dust which was highly poisonous, the covering being sufficiently transparent to see through it. He also stated that when lead was melted, a noxious vapour of a deadly nature was discharged, which was especially lethal to dogs.

The dangers of supplying drinking water through lead pipes are clearly shown by two Latin authors: Palladius is quoted by Adams (1846): "Ultima ratio est, plumbeis fistulis ducere, quae aquas noxias reddunt: nam cerusa plumbo creatur attrito, quam corporibus nocet humanis." Vitruvius (about 20 B.C.) is very similar: "Water is much more wholesome from earthenware pipes than from lead pipes. For it seems to be made injurious by lead because white lead is produced by it; and this is said to be harmful to the human body". Also "Water ought by no means to be conducted in lead pipes if we want to have it wholesome."

Macleane (1853) in his edition of Horace (65-8 B.C.) comments that the use of lead pipes for conveying water is referred to in an inscription concerning a supply to Venafrum. The use of such pipes had been disputed but this inscription confirmed that the line

"Purior in vicis aqua tendit rumpere plumbum"

referred to the purity of water from lead pipes.

Adams' (1846) Commentary on Paulus Aegineta included the note "Galen even mentions that water conveyed in leaden pipes sometimes proves deleterious by occasioning dysentery (Med. sec. loc. vii). Aetius makes the same observation (xi. 45)."

In France, Citois (1617), in a description of the "Colica Pictonum" mentioned small frequent stools often occurring along with constipation.

In Scotland, in 1754, Wilson discussed an illness to which all the inhabitants of Leadhills were subject, but particularly the men engaged in lead smelting. The milder stages were associated with an uneasiness and feeling of weight in the abdomen and sometimes colicky pains. The legs felt feeble and numb. There was anorexia, debility and laziness. "Sometimes diarrhoea makes a cure, but if it continues too long it is very hurtful." At this stage, the

sick were still able to go about and work. Then followed a "fixed" pain, constipation, giddiness, coma and delirium. He had seen birds, cattle and sheep die from grass or water contaminated with lead. The symptoms were like those of man. He described the terminal stages in dogs and since he could not get permission for a post mortem examination on any man who died of this condition he gave his post-mortem finding on a dog.

Tronchin (1757) stated that the epidemic of lead poisoning which was raging in Amsterdam was due to the change in building construction from tiles to flat lead roofs. The autumn leaves were carried on to these roofs by the wind and macerated there by the stagnant water which then acted on the lead before being carried off by rainwater into the cisterns. He observed that places which had no lead, no trees or no wind had less colic.

Baker (1767) gave a very clear exposition of an association between the endemic colic of Devonshire and the local peculiarities in cider manufacture associated with the use of molten lead as a filling for gaps in the cider presses or in some cases the use of presses lined entirely by lead. He supported his observations and theories with chemical studies. He also made the observation that among painters and other lead workers "some are cured by a spontaneous looseness of the belly".

In 1839, Tanquerel des Planches published a remarkably complete treatise on lead poisoning. This contained a great amount of detail extending to over 1,100 pages. He made observations from a series of over 1,200 cases of lead poisoning. Certain of these are relevant to the present studies. He observed a seasonal variation in the incidence of lead colic. This occurred in workers in industry much more frequently in the summer. His mortality

peak in July was three times greater than that occurring in December. He is not in harmony with later writers, certainly in Britain, in stating that women get colic less often than men. He attributed this partly, but not only, to women having less exposure than men.

Prodromal symptoms were described in detail in this work, as features of early lead intoxication which were recognisable prior to the occurrence of colic. He noted the occurrence of jaundice, a sweet taste in the mouth, a weight in the epigastrium and dull colicky pains elsewhere in the abdomen. The appetite was diminished and finally was completely gone. There was progressive constipation. Borborygmi and eructations were frequent. The workers could have these symptoms for days, weeks, or even months. Sometimes they were not continuous but intermittent at greater or less intervals, lasting for hours, days, or even a week at a time. He observed that sometimes an excess of alcohol, of food, or of work could precipitate an attack of colic. An attack of diarrhoea soon followed by constipation sometimes gave warning of an impending attack of colic. Patients tended to be morose, easily fatigued and suffering from disturbed sleep, and many suffered from neuralgic pains in the limbs. He discussed at some length the question of gaseous distension and eructations which occurred so frequently in the condition. From his very large series of cases of lead poisoning, Tanquerel des Planches stated that in round figures for every fourteen cases of lead poisoning twelve will have colic, eight "arthralgia", two paralysis and one encephalopathy.

De Mussey (1849) described an epidemic of lead poisoning at Claremont in Surrey. Of thirty-eight inhabitants of the establishment involved thirteen were attacked, eleven men and two women.

Six children aged from 3 to 7 all escaped. The water supply was delivered from a spring through two miles of lead pipe. From the study of this group, who had simultaneous exposure, De Mussey was able to comment on cases with varied and atypical symptoms . For example, some showed a marked nervous irritability and a surface hyperaesthesia of the whole body. Of interest in connection with the present studies is the comment that he tested the water with a solution of sulphuretted hydrogen, but it failed to produce any precipitate, though several samples sent to London subsequently showed a considerable quantity of lead. He mentions a figure of 1 grain per gallon, that is, 14 parts per million.

Christison (1845) described the danger of long lengths of lead pipe and very "pure" water supplies. He cites experiences in Dumfriesshire, Banffshire and Aberdeenshire, but was quite satisfied about the perfect safety of the lead cisterns and service pipes used in the City of Edinburgh, because water remained in contact with lead piping rarely for more than a single day. If, however, lead was kept in contact with the Edinburgh water for a considerable length of time the amount of lead taken up by the water might be considerable. He observed that when the quantity of lead did not exceed a 600,000th or a millionth part of the water it was ridiculous to imagine that any harm could result to man. Another of Christison's comments was that rain or snow water should not be collected from leaden roofs nor preserved or conveyed in lead piping and the same rule applied to waters of unusual purity with a low content of sulphates, carbonates, or chlorides. These observations on the Edinburgh water supplies of course refer to the relatively hard waters of the Pentland Springs.

The soft water Moorfoot supply to Edinburgh was not opened until 1879 when there were many complaints of the peaty discolouration of the new water supply. Colston (1890) quotes the popular epigram "tis true, 'tis peaty, and pity 'tis, 'tis true". Suggestions that the water was quite unwholesome prompted an authoritative report which stated that the new water supply was of excellent quality and well adapted for the supply of the town. While Gladhouse water was more strongly coloured than the other parts of the Edinburgh supply, it could not be called a very highly coloured water - "the colour is certainly of vegetable origin and cannot be regarded as injurious".

Some of the detailed observations of Alderson (1852) are of interest in showing the extent of knowledge at that time. He mentioned that no lead had been discovered in the various secretions and excretions of patients suffering from lead colic, but in one instance lead had been detected in the milk of a cow which had accidentally taken a large quantity of white paint. He observed that hair dyes contained lead, a practice which continues to the present day ("Which" 1960). Adulteration of cider and wine with lead was mentioned and the contamination of beer passing through lead pipes and especially left lying in the lead pipe overnight.

Alderson made lengthy comments on poisoning from water supplies passed through lead pipes and lead storage cisterns. He observed that some of the phenomena are hard to explain and harder still to prevent. Apparently, at this time, the Board of Health had made a statement on the benefits likely to result from the provision of a pure soft water supply for the citizens of London. The chemists of the existing water companies were concerned by the fact that

the degree of lead solvency seemed to be proportional to the purity of the water. An official government commission of three chemists had been set up to study this matter. The conclusion of the commission, that the solvent action of the water on lead piping existed only in an almost imperceptible degree, was at direct variance with the clinical observations of Alderson and his colleagues. Alderson noted that the sediment in water supplies might carry down lead, having the same effect as a filter, but that stirring up of such sediment could have the opposite effect. He specifically mentioned the effects of a shower of rain stirring up the impurities, and that the black sediment contained lead in large quantities. His conclusion, therefore, was that if soft water was to be introduced a special study must be directed towards devising a new mode of distribution and the use of lead must be abandoned.

References to the problem of plumbo-solvency were made in the annual reports of the Local Government Board. In 1890, it was estimated that upwards of 6,000 persons in the West Riding of Yorkshire alone appeared to be liable to lead poisoning by the drinking of water supplies in their districts.

Power (1894), in the 23rd Annual Report of the Local Government Board, stated that in the West Riding of Yorkshire, Lancashire, Cumberland and Westmorland there was a population of over six million. Of these between seventy and eighty per cent had mains public service water from moorland sources. He noted a wide difference in incidence of lead poisoning. In the West Riding of Yorkshire this was abundantly recognised. In Lancashire it was hardly heard of, and in Cumberland and Westmorland there was none. He observed that "the want of recognition of lead poisoning has perhaps had a not unimportant influence

on the favourable report rendered of certain supplies by the local officers." He also observed that since his enquiries, cases had begun to be recorded in the areas previously regarded as free of lead poisoning from this cause.

Observations on Plumbo-Solvency and Lead Effects in the Present Century.

A valuable contribution on the subject of lead poisoning in water supplies was made by Houston in 1902 in an extensive study of moorland water supplies in Lancashire and Yorkshire. Thirty-five out of fifty-eight reservoirs examined were found to contain acid water with plumbo-solvent properties. Some of Houston's observations were that moorland gathering grounds of water supplies are usually rich in peat and that moist peat invariably yields an acid reaction. Though the water from peat is always acid, the degree depends on the amount of peat and the length of time the water has been in contact with it. Acid water dissolves lead and the degree of plumbo-solvency was mainly, in Houston's view, regulated by the amount of the acidity. Moorland spring water, on the other hand, is usually neutral. During dry weather and especially towards the end of a period of drought, moorland supplies being chiefly of spring origin are usually neutral, but during wet weather, especially after storms of rain, moorland supplies are much more acid and especially so after a spell of drought.

Remedies suggested for the prevention of plumbo-solvency are the elimination from reservoirs of water draining from especially peaty areas, the provision of "leaping-weirs", contrivances which automatically reject the first washings of peat after periods of drought, and neutralisation of acidity by adding a thin layer of slaked lime to the surface of the sand filters and beneath the sand a layer of limestone.

Glaister (1910) described cases of lead poisoning in Vienna occurring in 1905 which were traced to the repairing of burst water pipes with solder. Contact of the water with six inchhs of pure lead was found to make the water unfit for human use, but Glaister mentioned that altogether 3,764 analyses were made of which more than 3,000 showed the water to be free of lead. In about 100 samples, there was found 1 p.p.m. of lead, in 50 samples 2 p.p.m. and in 25 samples 3 p.p.m. Glaister lists a number of places in Britain where plumbo-solvency had been noted - Sheffield 1887, Halifax 1901, Birmingham, Aberdare, Wales 1908 (including six deaths), Saddleworth, Yorkshire 1907, Pontypridd and the Rhondda Valley 1904 to 1906. These were all dealt with by addition of chalk or lime to reduce this plumbo-solvent effect.

In 1911, Sir Thomas Oliver stated that serious symptoms arose in one of his own cases from drinking water which contained 0.04 p.p.m. of lead (0.0028 gr. per gallon). He also mentioned that lead entering the gastro-intestinal canal is acted upon by the gastric juice, the hydrochloric acid of which is sufficient to convert a quantity into soluble chloride. During the simultaneous digestion of protein only a very small quantity of lead is dissolved.

Wright, Sappington and Rantoul (1928) studied 102 water supplies in Massachusetts. All the waters analysed contained lead and the lead content was most strikingly related to the carbon dioxide content. There was no apparent relation between length of pipe and lead content. A total of 253 persons using 90 of these water supplies had clinical investigations and of these 63 or 24.9 per cent. were poisoned according to the criteria used, which seem adequate. They record that poisoning occurred among fourteen persons ingesting as little as 0.1 mgm. of lead daily over an

average period of 8½ years. Of special interest is their recording of twenty cases of lead poisoning out of 65 persons exposed to water, having a lead content ranging from 0.05 to 0.1 mgm. per litre, an incidence of illness of 30 per cent. of those exposed. Clinical details are given of three of these patients. A further three persons are listed as poisoned out of 24 drinking water containing less than 0.05 mgm. per litre, but no clinical details are given of these particular cases.

Davidson, Fullerton, Rae and Henderson (1933), stated that poisoning from lead piped water supplies was a subject which had been regarded as of purely historic interest. They found, however, that of 160 houses in Aberdeenshire supplied with long lengths of lead piping, 108 had a lead content in excess of 0.5 p.p.m. The only practical remedy they were able to suggest was the prolonged running of the tap each morning before water was used for drinking or cooking purposes.

Picard (1934), at this time in Britanny, listed 66 cases of lead poisoning from soft waters, most of which occurred within 2½ months of the installation of new lead piping or pumps. He describes this as "un véritable péril social".

A paper on "The Action of Water on Lead with Special Reference to the Supply of Drinking Water" was published by Ingleson (1934). This was described as a summary of existing knowledge and contained 115 pages and 371 references. He stated that any water delivered through lead pipes might be expected to contain lead, although the amounts might be in many cases so minute as to be of no practical significance. Lead determination in the water of an area where plumbism is suspected was not generally of much value

in attempts to fix the permissible limit of lead content since the samples were often taken after, but not during, the period when lead absorption was occurring. So many factors, apart from the condition of the pipe and the properties of the water, affect the amount of lead withdrawn in a sample of water, that comparable values are difficult to obtain. He stated that the period of stagnation of the water before sampling, the nature of the lead compound produced, the shape, size, and density of the particles suspended, the rate of sampling, the slope of the pipe, and the position of the tap relative to the pipe, all have an important influence on the proportion of the total corrosion product withdrawn with the sample. Pressure and temperature exert an influence by affecting the rate of separation of bubbles of gas on the walls of the pipe. The length of the piping may influence the lead content, but does not always do so. Two consumers, with apparently similar supplies might be receiving very different amounts of lead in their water.

Ingleson gives the solubility of lead compounds in water in p.p.m. as:

Lead Chloride	6955.2 ($PbCl_2$)
Lead Hydroxide	93.15 ($Pb_3O_2(OH)_2$)
Lead Carbonate	0.04 ($PbCO_2$)

He stated that the nature of acids (other than carbonic acid) from peaty moorlands was not known. His criticism was that various chemical substances had not been isolated under conditions prevailing at the gathering grounds and, therefore, their presence is inferred rather than proved. Such substances are hydroxy-stearic acids, various amino acids, oxalic, succinic and acrylic acids. Phosphoric, acetic, malic and sulphuric acids occur in some humus. L-leucine (d amino-p-methyl valeric acid) and d-isoleucine (a amino-p-methyl valeric acid) had been extracted from brown American peat in a state of

purity but "humic" and "ulmic" acids were still the subject of much argument as to their nature. This paper for all its comprehensiveness gives very indefinite conclusions as to the safety limit for a lead content of water and quotes an extremely wide range of opinions on the subject.

Suggested mechanisms for the attack of water on lead (Liddiard and Bankes 1944) include the formation of lead hydroxide which is subsequently converted into insoluble basic lead carbonate in the presence of carbon dioxide. This causes a protective film on the surface of the lead. Increasing amounts of carbon dioxide cause the amount of lead in solution to rise due to the formation of lead bicarbonate which is comparatively soluble.

The dangerous potentialities of the acid nature of moorland waters in dissolving lead had been well recognised. Miles (1948) demonstrated very clearly that another major factor in the degree of attack on lead piping is the organic content of the water. Many waters suspected of being plumbo-solvent are soft upland waters carrying peat extracts of collodial organic matter.

Opinion in Britain on the subject of plumbo-solvency may be judged from the comments in a standard work of reference "The Examination of Waters and Water Supplies" (Thresh, Beale and Suckling, 7th Ed. 1958). This states that the intake of lead which can be regarded as safe for all sections of the community cannot be definitely stated, but in view of the possibility that an extremely small habitual intake of lead in drinking water may cause symptoms in certain hypersensitive individuals, its complete absence would seem advisable. Therefore 0.1 mg/litre (p.p.m.) should be the limit for lead in drinking water, but where lead piping is installed the concentration of lead in the water after prolonged contact with the

pipes might be higher. In no instance, however, should the concentration of lead exceed 0.3 mg/litre after 16 hours contact with the pipes.

Other observations from this work are that factors which determine the action of plumbo-solvent waters on lead piping are complex and not fully understood and no strict correlation between cause and effect has been established. Among the factors involved are listed:

1. pH value and acidity,
2. Calcium and magnesium bicarbonate content,
3. Organic purity of the water,
4. Variation according to climatic conditions,
5. Treatment applied, if any,
6. Possible development of a protective coating on the pipes in time.

It is noted that the action of water on lead may be more serious with hot water than with cold, and that drawing hot water first thing in the morning from a lead piped system has given rise to lead poisoning for this reason. A reference is made to an experiment by Houston at the beginning of the century which demonstrated that one acid water took up over 25 p.p.m. of lead in 40 seconds and therefore rapid transit of water through pipes is no protection. Another observation in this large work is that modern water works practice includes the stripping of beds of peat from an area to be used for a new reservoir.

In the United States, the Public Health Service had for many years a limit of 0.1 p.p.m. for lead content of drinking water. This was attacked by Kehoe (1947) whose opinion was that while this did not cause undue hazards under ordinary circumstances, it was too high for that segment of the population which required to take in much larger than ordinary quantities of water per day in order to maintain water balance. Persons who must live and work at high temperatures could increase their water intake many fold and in these circumstances there might well be a potentially

dangerous intake of lead. The U.S. Public Health Service limit for lead content was reduced in 1960 to 0.05 mg/litre (p.p.m.).

A Committee of the American Water Works Association (Bean 1962) suggested that in place of a standard limit there should be a concept of an ideal water supply. With regard to lead, this Committee considered that this cumulative poison was associated with a dependable excretion of 0.3 to 0.5 mgm. per day though there might be some retention of lead of the latter amount. An ideal of 0.03 p.p.m. at two quarts per day would limit the intake of lead from water to 15 per cent. of a maximum allowable total daily intake.

The World Health Organisation in 1958 adopted the level of 0.1 p.p.m. as an international standard for a limit of lead content in drinking water. In 1963 this standard was reduced to 0.05 p.p.m. There is no legal standard in Britain for the limit of the lead content of drinking water.

Against these American and international standards, we must consider the statements of Wood (1961) that the adoption of the standard of 0.1 p.p.m. in Britain would raise very serious problems. He stated that we should now have to regard almost all public supplies in Britain as plumbo-solvent, if the term is to be defined as meaning that the water is capable of dissolving more than 0.1 p.p.m. of lead from lead pipes under certain conditions. If such a limit is necessary, then there is need for much investigation by water undertakings of the extent to which lead can be picked up by their supplies. It might be, that in some areas at least, the use of lead pipes for drinking water would have to be forbidden. He appealed for an official pronouncement on whether a limit of 0.1 p.p.m. was too stringent. This would avoid much anxiety on the part of those responsible for water

supplies and perhaps the expenditure of considerable sums of money.

Another comment on plumbo-solvent tendencies of British water supplies has been made as a result of statistical studies demonstrating a relationship between softness of local water supplies and mortality from cardiovascular disease. Such studies have been made in Japan, by Schroeder (1960), in the United States, and by Morris, Crawford and Heady (1961) in respect of England and Wales, and in all of these it has been found that the softer the water supply, the higher the local death rate from cardiovascular disease.

Hoather (1961) commenting on these last observations, which were made concerning the County Boroughs of England and Wales, put forward the opinion that the cause might be the life long consumption of waters not protected sufficiently against plumbo-solvent action. Thus amounts of lead too small to cause recognisable lead poisoning might be a factor in causing cardiovascular disease. He noted that water having a low temporary hardness and a pH of less than 7 had, to some extent, a plumbo-solvent tendency which might be increased by organic matter of peaty character. He observed that many large water supplies of County Boroughs showed plumbo-solvent characteristics and for some of these treatment to raise the pH was commenced very recently.

Cox(1964) goes much further than this. He states categorically that toxic effects are noted when the lead content of water supplies exceed 0.05 p.p.m. Lead piping should not be used with waters having pH values of less than about 7.8. Lead piping may be used with waters having pH values between 7.8 and 9.6 provided that there is an assurance that this pH range will be maintained. These opinions are published in a World Health Organisation manual prepared in consultation with "24 specialists in various countries". They present formidable problems

for British water undertakings. The maximum pH value for example for any of the Edinburgh water supplies in the year 1960-61 was 7.7, with average figures ranging from 6.9 to 7.4. From the most explicit recommendations by Cox we would have to regard these supplies as unsuitable for use with lead piping unless they received further treatment.

The literature on the subject of plumbism from water supplies and from industry accumulating through the years is now very extensive indeed. There have been, and continue to be, differences of opinion, but there is a general trend towards the reduction of intake of a known cumulative poison. With copper and polythene available for piping we are now at the stage when lead can be abandoned for domestic water supplies as advocated by Alderson a hundred years ago. While it would not be difficult to prohibit the use of lead piping of water supplies in all new buildings erected in areas where the average water pH was less than 7.8 the great difficulty is to demonstrate whether there is any need or any urgency for water treatment or plumbing alterations in the innumerable lead piped domestic supplies in Britain which are already receiving such water.

Among the great number of publications on the effects of lead are a number of important reviews. While some part of these reviews will be discussed under the heading of Symptoms and Signs of Plumbism their importance demands that they should be included in any description of the history of the subject.

Legge and Goadby (1912) wrote a complete treatise on industrial plumbism. Their observations ranged from experimental studies on the solubility of lead compounds in human gastric juice, through an analysis of the statistics and clinical features of

the 5,637 cases of lead poisoning reported by factory surgeons between 1900 and 1909, to detailed pathological studies and experimental evidence of the results of feeding experiments, innoculation, and inhalation experiments with lead in animals. The symptoms of the various forms of lead poisoning and the chemical investigations which were possible at that time, were dealt with and also the treatments available. In addition to chapters on preventive measures against lead poisoning there are detailed descriptions of the various processes involving the use of lead and lead compounds and the hazards associated with them.

The results of studies by another team of investigators were consolidated by Aub, Fairhall, Minot and Reznikoff (1925). This group demonstrated that there was an analogous metabolism of calcium and lead. Lead circulating in the blood is stored in the skeleton and conditions which favour the deposition of calcium in the skeleton also favour the deposition of lead. Likewise, there is an increase in the excretion of stored lead parallel with any increased excretion of calcium. Among other observations, these authors suggested that susceptibility to lead palsy depended on the chemical reactions between lead and the metabolic products formed during muscular activity.

Cantarow and Trumper (1944) gave a review of the literature on the subject of the lead content of blood. They agreed with various authors that it was logical to assume that clinical manifestations of lead intoxication should be more directly related to the concentration of lead in the circulating plasma than that contained in the red blood cells. The lead in the red blood cells being in comparatively firm combination would not be expected to exert a toxic effect on the tissue cells. They felt, however, that the difficulties inherent in the methods of separation of cells and plasma precluded the possibility of securing exact

information regarding the distribution of lead in the circulating blood. They stated very clearly that the data they reviewed indicated that the concentration of lead in the blood bears no consistent relationship to the appearance or severity of clinical manifestations of lead poisoning. The latter may be absent with high levels of blood lead and may be present with low levels. In their opinion, therefore, the diagnosis of lead poisoning must depend on the presence of clinical manifestations of that condition and the demonstration of lead as an aetiological agent. The demonstration of an abnormally high concentration of lead in the blood is of course of great value in the presence of such symptoms in establishing the diagnosis. Since the presence of abnormally large amounts of lead in the blood is a result either of fresh absorption or of mobilisation of previously stored deposits, they mention the medico-legal importance of the fact that active mobilisation of lead from the bones with the development of episodes of acute intoxication may occur months, or even years, after the unusual exposure to the lead has ceased.

The Milroy Lectures on "The Care of the Lead Worker" by Lane (1949) included a defence of the fact that, in this country, chronic renal changes have been accepted as sequelae of industrial lead poisoning and have ranked for compensation accordingly. He considered that the diminution in the frequency of such cases is due to the great improvement in the working conditions which now prevail. He also discussed the fact that women are excluded by law from work involving the more serious lead risks. His conclusion on this subject is that the evidence must be accepted that given sufficiently large doses women are more likely to develop lead poisoning than men. The fact that under these circumstances, they are more likely to abort or lose their children in the first year of life, is

established beyond doubt, and the wisdom, therefore, of excluding women from the dangerous lead occupations is manifest.

Kehoe and his colleagues in Cincinatti have published a number of papers on various aspects of the absorption, excretion and toxicity of lead over the years from 1933 to 1964. The most important of these observations have been collected in his Harben Lectures (1961). One of these is devoted completely to the normal metabolism of lead, and the second mainly to experimental studies of the inhalation of lead compounds. The third ranges from discussion of the diagnosis of lead intoxication and on lead poisoning in children to comments on occupational hygiene in the lead using industries and much more general observations on exposure to lead in the realm of public health. This last section includes comments on the limit of safety for a total lead intake per day over a prolonged period of time. This is based on experimental evidence and is most valuable. This author, however, seems unduly dogmatic in suggesting that even the mildest type of lead poisoning does not occur with a blood lead concentration below 80 µg per 100 G. He makes the specific exception that with tetra-ethyl lead the concentration of lead in the blood bears little or no relationship to its absorption and distribution in the tissues. His views are directly opposed to those of Cantarow and Trumper which have already been quoted, but he does concede subsequently that the onset of intoxication often coincides with a sharp increase in the rate of absorption or mobilisation of unbound or ionic lead.

Apart from these major reviews, a great number of papers have been published on problems produced by the toxicity of lead. The international nature of the hazard is evidenced by contributions from many countries, some of them concentrating on one or other

aspect of the subject. It is impossible to do more than mention some specific problems which are relevant to the material to be presented subsequently and refer to some of the observations which have already been made on these.

There is one well recognised form of lead intoxication which may present as an acute toxic psychosis with a manic state. It may be impossible to differentiate from a catatonic schizophrenia, without a good occupational history confirmed by a laboratory finding of excessive lead in the urine (Zavon 1964). In this there is no fall in haemoglobin or red cell count, no rise in punctate basophil cells, and there is apparently no effect upon the porphyrin metabolism (Sanders 1964). This is "organic lead intoxication" - a term which is used in connection with poisoning with tetra-ethyl lead. Browning (1961) believes that the volatile organic lead compounds have a special predilection for lipoid and nervous tissue. The symptoms are of insomnia, terrifying dreams, emotional instability, and increased and erratic physical activity. There is anorexia, vomiting and instead of constipation, there is more likely to be diarrhoea. As already mentioned, Kehoe describes the use of blood lead estimations in this condition as futile. The urine in tetra-ethyl lead intoxication is likely to contain considerably higher quantities of lead than is usual in cases of poisoning from inorganic lead compounds, since lead absorbed in this form is more rapidly excreted.

Studies of tetra-ethyl lead and its use in petrol have been carried out over the last thirty years and more than a third of the extensive proceedings of a symposium in the United States in 1964 was devoted to this.

Early work with radioactive isotopes of lead (thorium B) by Behrens (1925) was continued by Fees (1932), who found that over 90 per cent. of the ingested lead was rapidly absorbed from the intestinal tract. This study was done with mice giving doses corresponding to 15 to 18 mgm. daily for men. Previous studies had used very much bigger doses and she considered that most of the lead in these passed out in the faeces unabsorbed. At this dosage, when the mice were killed and dissected after one hour only 5 per cent. of the ingested lead remained in the gut, and 91 per cent. was distributed through the rest of the body. If the mice were not killed for 27 hours, however, 25 per cent. of the lead was found in the gut and 50 per cent. in the rest of the body, the remaining 25 per cent. having been eliminated in faeces and urine. In these experiments, however, no food was given. Her colleague, Miyasaki (1930), had demonstrated that food inhibited the absorption of lead to some extent and milk considerably inhibited this absorption.

Apart from variations in absorption produced by food and milk in the gut, some of the absorbed lead is returned to the small intestine through the bile duct (Aub, et.al. 1925) and fails to gain access to the general circulation. These factors probably account for other very different statements of the amount of lead ingested which is actually absorbed. The observations of Fees are described to demonstrate that, in appropriate conditions, a very high proportion of the ingested lead may be absorbed.

From Queensland, evidence has been presented by Nye (1933) and Murray (1939), that a major factor in the causation of the abnormal incidence of chronic nephritis in that State is lead poisoning in childhood. In this instance, the source of the lead was lead paint on the railings of verandahs. It was not that

the children were suspected of chewing the paint, as has happened with lead painted toys, but rather that the effects of heat and sunshine caused the paint to come off readily on the hands of very young children clinging to the railings. More recently, in Yugoslavia, cases of nephritis were also recorded in a community where widespread lead poisoning had occurred because flour had been ground with millstones which had been repaired with lead. In six of these cases, treatment with Penicillin caused a rise in the level of lead in blood and urine to a level of at least three times the original. The greatest increase in urine was from a 100 µg/litre to 1100 µg/litre. Mokranjak and Soldatorri (1958) extended their observations on the mobilisation of lead by antibiotics by animal experiments which demonstrated that in sheep which were fed with lead until their blood lead level was 220 µg/100ml. administration of Terramycin (Oxytetracycline) produced a rise of blood lead level to 720 µg/100 ml.

Studies of pregnancy by Bell, et.al. (1925) and Datnow(1928) demonstrated that in early pregnancy, lead damaged the chorionic villi causing a coagulation necrosis. Porrit (1934), published a theory that lead was a significant factor in eclampsia, based on a statistical study of maternal mortality from this cause and the geographical distribution of soft water supplies. The reviews on this book ranged from the Lancet - "the reader cannot fail to be impressed", and the Journal of Obstetrics and Gynaecology which gave a number of critical objections, but said "this is an interesting idea", to the British Medical Journal which gave quite a scathing review and stated that "it would seem very improbable that the Public Health Service can have overlooked a latent form of plumbism due to potable water".

The first observation of the occurrence of porphyrin in the urine of a patient with lead intoxication was made by Binnendijk in the early 1880's according to Haeger-Aronsen (1960). The various steps by which this observation developed until it became a recognised screening procedure in industrial medicine have been described by Shiels, Palmer, Cornish and Kearley (1953), but they omit to mention that urine coproporphyrin excretion was extensively used as a screening test in 1939 by ten Berg and Grotepass as part of the study of a population exposed to lead poisoning from drinking water. The lead hazard in that instance was considerably greater than that involved in the present study. Of 212 pumps from 198 wells, 65 per cent. of the pumps were rejected, because the lead content exceeded 0.3 mgm. of lead per litre. Excluding the many persons studied who used those supplies there remained 273 who used water containing less than 0.3 mgm. per litre, but even a water lead content less than 0.1 mgm. per litre, after lying for 10 hours in a lead pipe, caused a great number of persons to show an increase in porphyrin excretion. The authors concluded that even a lead content of less than 0.1 mgm. per litre might be dangerous for human beings, but found themselves unable to give an absolute limit above which the lead content of drinking water becomes injurious for man. For a large scale examination of a population with regard to injurious effects from the water supply, estimation of coproporphyrin in the urine was preferred to examination for punctate basophilia. They demonstrated by human experiments giving water containing lead in various concentrations that increased excretion of coproporphyrin preceded the development of punctate basophilia. As a remedy, for these dangerous water supplies, they suggested the introduction of a central water supply for the population, but noted that their observations were likely to apply also to other communities in four different districts in Holland

where lead poisoning had already been noted. A further report on this study was given by de Langen and ten Berg (1948) under the title "Porphyrin in the urine as a first symptom of Lead Poisoning".

A number of papers have appeared since then on the reliability of urine porphyrin tests and the usefulness of these in evaluating lead exposure. Johnston and Whitman (1952) used de Langen and ten Berg's (1948) method and found a good correlation between urinary lead and fluorescence.

Harrold, Meek and Padden (1962) described a modified urinary porphyrin test as probably the one outstandingly reliable means of demonstrating the presence of lead damage in the animal organism. These authors commented that the fluorescence is itself a sensitive indicator of damage, whereas lead in either urine or blood is an indication of absorption, transport or removal of lead within the organism. Therefore, determinations of blood or urine lead while useful are one step further removed from the actual indication of damage to the individual. They also comment that increasing the complexity of the test serves little useful purpose and destroys much of the practical value of it to the physician both in his office and in large scale screening programmes in industry.

Shiels, et.al. (1953), point out that urine coproporphyrin tests have certain advantages over the other tests used in routine control of employees exposed to lead hazards. The first is undoubtedly the speed with which the test can be performed. The second major advantage is that accidental contamination of the sample with lead is of no significance. It is also much less tedious than the performance of a large number of punctate basophil counts. The disadvantage is that porphyrin in urine is not stable under the influence of light and samples must be kept in amber coloured bottles or in the dark. These authors

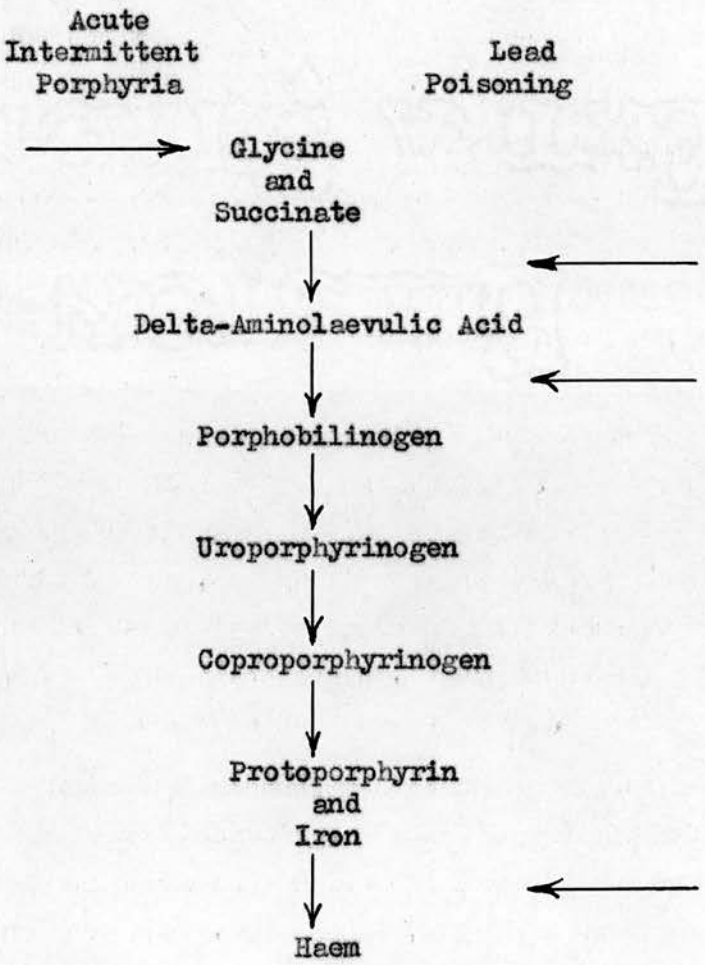
assess the correlation between blood and urine lead estimations and punctate basophil counts and urine coproporphyrin findings and consider that as an aid to diagnosis in doubtful cases it is not advisable to abandon the other tests, but to do all three tests in addition to the coproporphyrin test.

Vanotti (1954) was of the opinion that lead poisoning causes an inhibition of the utilisation of iron in the synthesis of haemoglobin. This inhibition causes the formation of a blood pigment minus iron, a porphyrin of the type 3. By 1955, Wylie was able to list eight different modifications of tests for coproporphyrin which were in use in industry. Donath (1956) has described a simple portable apparatus for use by the industrial physician. Details of this are given in the section on methods available for the study of lead exposure.

Goldblatt and Goldblatt (1956) stated that there is no doubt that the order of appearance of the blood phenomena important in the clinical diagnosis of lead absorption, is coproporphyrinuria, increase in blood protoporphyrin and non Hb iron, punctate basophilia, fall in haemoglobin and fall in the number of red cells. In lead absorption, coproporphyrinuria is a sign of the first importance from diagnostic, preventive clinical and medico-legal aspects. It has great clinical value because of its constancy, its intensity, its early appearance and its persistence.

Haeger-Aronsen (1960) has described the urinary excretion of d-amino laevulic acid as being a more specific indication of increased lead absorption than urinary coproporphyrin excretion, but in the opinion of Goldberg (1965) this does not appear as rapidly in lead poisoning as an increase in urine coproporphyrin.

Dagg, Goldberg, Lochhead and Smith (1965) give a simple scheme of the possible sites of disturbance of haem biosynthesis (indicated by horizontal arrows) to show the different levels of effect in acute intermittent porphyria and lead poisoning. Uroporphyrinogen and coproporphyrinogen are the reduced forms of uroporphyrin and coproporphyrin respectively.



Other more complicated schemes have been suggested for the process of haemoglobin synthesis, but this seems sufficient for the present studies.

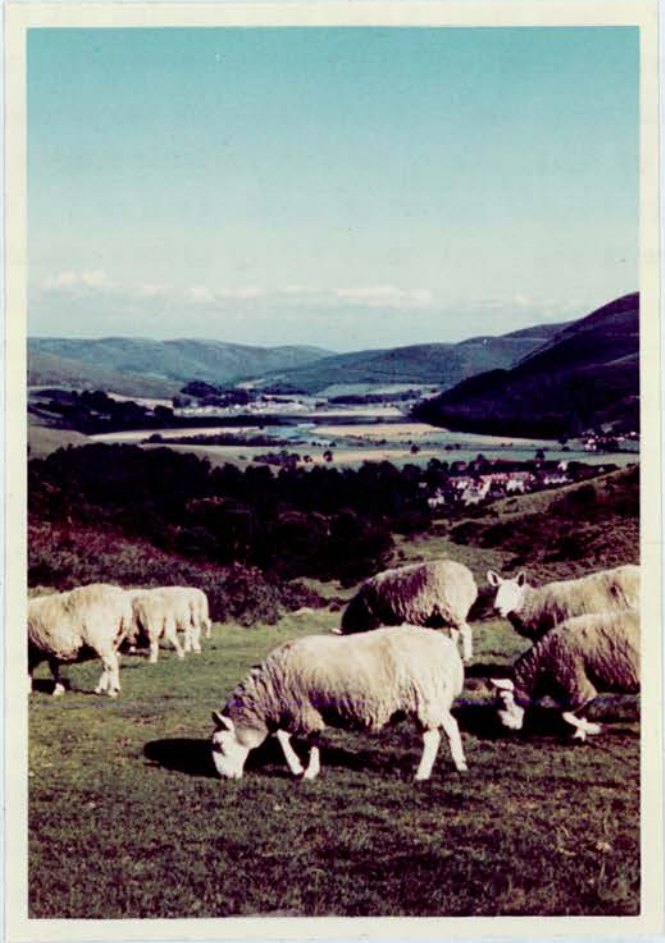


Plate 3.

The Tweed Valley - the area of the practice.

The Character of the Practice Area.

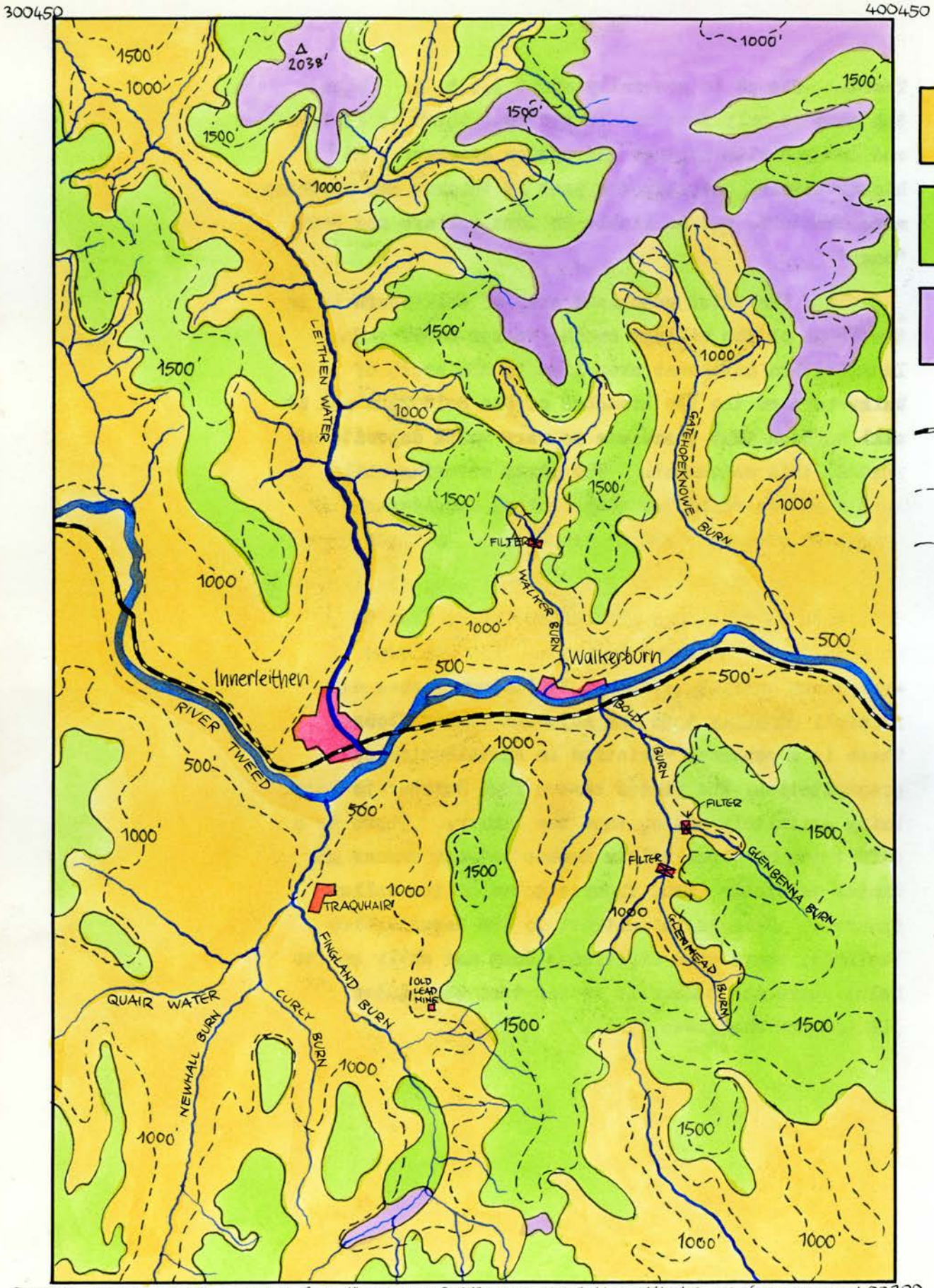
These studies have been carried out for the most part in a general practice in the eastern part of Peeblesshire, a small inland shire in the Southern Uplands of Scotland. This is predominantly a pastoral area with a small amount of arable land on the floors of the valleys. The steep valley slopes are broken by woods and plantations. The general appearance of the district is shown in Plate 3. Part of Innerleithen is in the centre with Walkerburn in the distance farther down the River Tweed.

Three main soil categories are described in the Innerleithen area - mineral soils, organo-mineral soils and peat (see Fig.1.). Apart from the peat they are derived from Silurian greywackes and shales. There is a regularity in the distribution of these soils. On the steep valley sides of the Tweed and its tributaries there are predominantly mineral soils up to 1,250 feet or thereabouts. Above this level on the flattened hilltops the organo-mineral soils occur, but at about 1,500 feet these merge into peat.

The mineral soils have little or no surface accumulation of organic matter. They are mostly acid stoney brown loams with a surface pH of about 4.5, unless they have been treated with lime. They are usually grass covered.

The organo-mineral soils have a surface accumulation of peat or raw humus between two and twelve inches thick under a thick mat of heather and coarse grasses. The surface layers are highly acidic with a pH range of 3.5 to 4.5 (Regg 1965). As they are mapped in Fig.1. the organic soils consist of an organic accumulation of true peat of more than twelve inches. This occurs only on high ground, particularly above 1,500 feet on the hills to the north of the

Figure 1.



Base map details are taken from 1" Ordnance Survey map. Nat. Grid co-ordinates are shown at corners.

SCALE IS 1 : 63,360 or 1" to 1 MILE.

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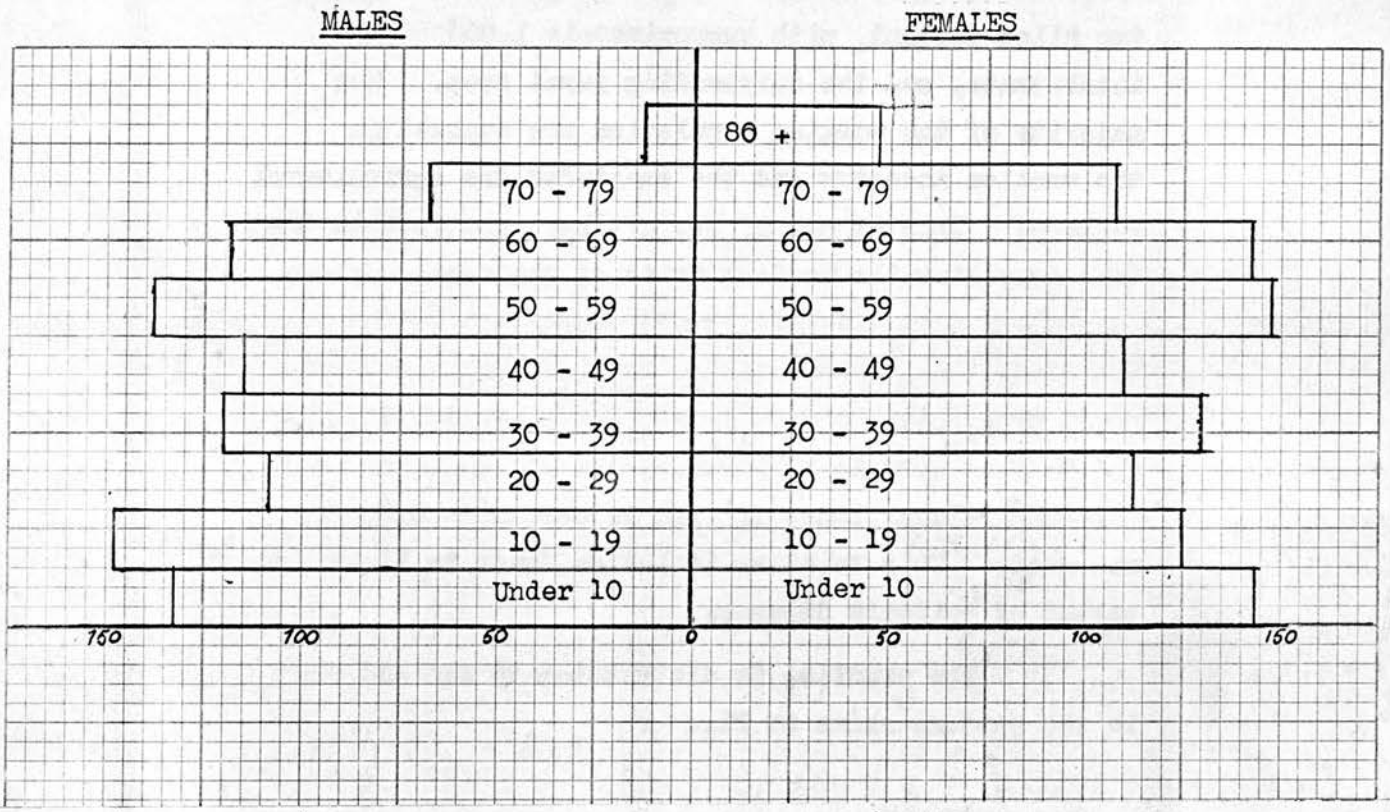
Tweed. The pH is generally about 3.5 to 4. When the peat is only from one to two feet thick it is firm and covered with heather and cotton grasses. At higher levels, however, the peat is thicker and contains more moisture, and is liable to form gulleys and peat "hags".

The water catchment area of Walkerburn is to the north of the village on the Walker Burn. The Innerleithen catchment area lies to the south of Walkerburn on the two branches of the Bold Burn and it will be seen that there are no very thick deposits of peat in this catchment. The peaty covering, while less than twelve inches deep, varies considerably in thickness even on adjacent branches of the same burn.

One feature of the rainfall characteristics of this area is the large and sudden change from the uplands to the adjacent valleys. The hilltops everywhere have at least ten to fifteen inches more rainfall annually than the adjacent valley floors. There is a seasonal variation in distribution of precipitation, the winter season from October to March being definitely wetter than the summer. There is a difference of three to six inches between summer and winter rainfalls (from figures taken at the valley floors). This is in contrast to the Berwickshire lowlands, where this difference does not apply and to Kelso where the summer is wetter than the winter (Linton and Snodgrass 1946).

Figure 2.



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The Composition of the Community Studied.

Except where otherwise stated the patients in these studies are from a single handed practice with 2,042 patients at 1st July 1963. They are drawn from the town of Innerleithen - population 2,278 at the 1962 Census - the village of Walkerburn, two miles distant, with approximately 1,000 inhabitants, and the surrounding rural area. The majority of the working population are engaged in the woollen industry and the remainder are agricultural workers. This is one of two similar practices in the town supplying the medical needs of the area. There is a small town six miles to the west, but to the east the nearest is fifteen miles, and both north and south population is very sparse for a greater distance. The nearest city is thirty miles to the north and only a very few travel there to work as communications are not good. This relative isolation tends to limit the spread of epidemic disease.

The practice is distributed by age and sex in the pattern shown in Fig. 2.

SECTION II

Methods of Study Available

General Practitioner Methods for the Investigation of Plumbo-Solvency.

It might reasonably be imagined that in this modern era the local authorities would have such control over the water supplies that it would be unnecessary for general practitioners to undertake any investigation.

The evidence presented in the section on water supplies, however, will give a very different picture. There are in Scotland many small privately owned water supplies. It would be an enormous task for Public Health Departments and Analysts to investigate any great number of these. County, Burgh, and especially City water supplies should be receiving adequate supervision and sampling but as will be described subsequently, some of the methods used for analysis fall short of modern standards.

There is a need for a simple test which a general practitioner could undertake in his consulting room to investigate whether a water supply tends to have corrosive effects on lead piping. He could then arrange for more elaborate and exact investigations if these seemed appropriate. It is the duty of the local authorities to take such steps as may be necessary to ascertain the wholesomeness of the water supplies within their districts(Water (Scotland) Act 1946, part 2, 7.) Such analyses are expensive and the County Council might object if asked to pay for a large number if the results proved negative. There is, however, a serious lack of a suitable preliminary screening method which is sufficiently sensitive to meet with modern requirements.

The simplest way in which the general practitioner might be made aware that the water supplies in his practice had an aggressive action on piping is not by a laboratory test, but by the observation of the presence of the blue staining of copper beneath

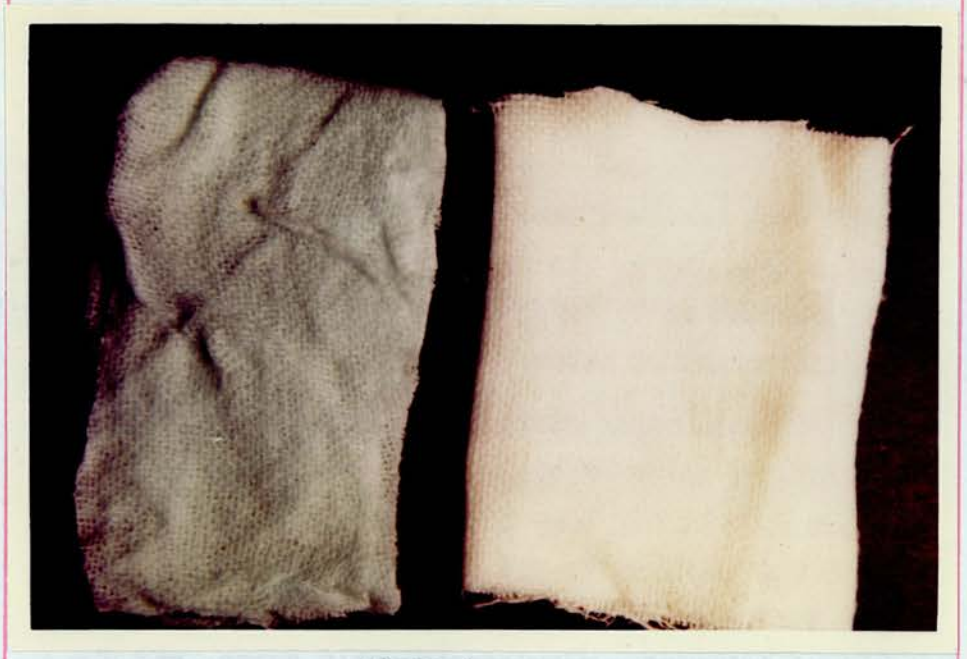

Plate 4.

Copper staining of a baby's face cloth after eight weeks in use. (The white of the original material has not reproduced well).

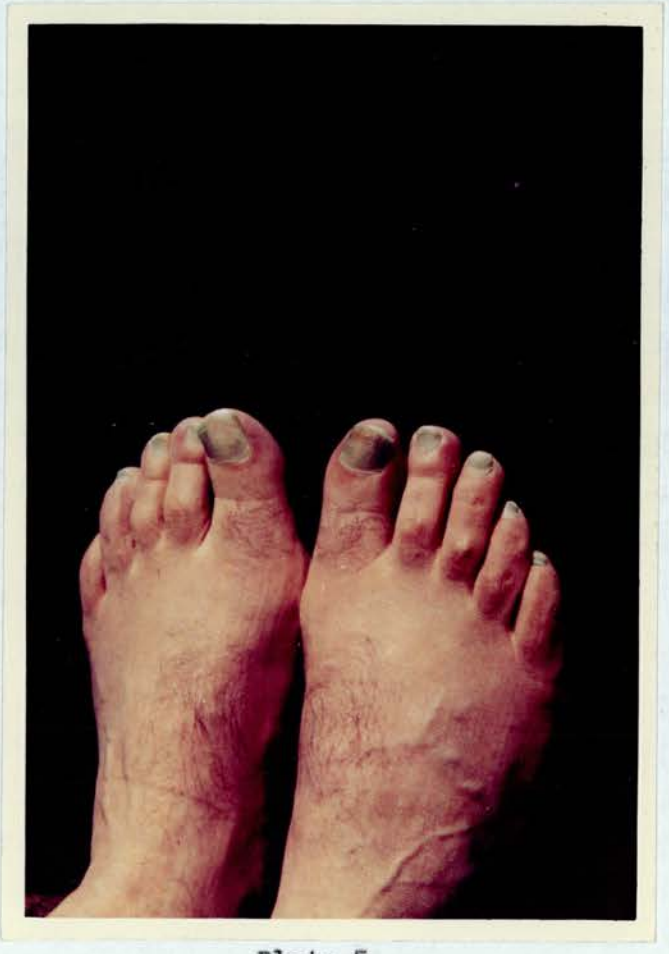

Plate 5.

Copper staining of toenails.

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the taps at baths and wash basins. If the general practitioner realised that this signified an attack not only upon copper piping but also on any lead piping present in the distribution system then his suspicions might be roused.

Some copper staining is due to precipitation of the copper salts by soap. One patient in this practice brought her baby for a routine immunisation when it was eight weeks old and mentioned that the baby's face cloth had turned blue. This suggested copper staining of a very considerable degre, and the face cloth was obtained. It is shown in Plate 4. along with a piece of the original white material, though the white has reproduced very badly in the colour photograph. The patient was told to stop using her hot water supply for filling kettles and water samples were forwarded for analysis. These were reported as containing lead in excess of 1 p.p.m. and copper 0.3 p.p.m.

An even more startling example of copper staining was provided by a farmer and his son in a neighbouring area whose toenails became bright green (see Plate 5). Iron staining of sanitary fittings might also give warning of aggressive action of water supplies, but the colour is less obtrusive than the vivid colouring of copper.

As we have already mentioned, Cox (1964) states that lead piping should not be used with waters having pH values less than about 7.8. The upper limit of the pH range of Bromothymol Blue Indicator is pH 7.6. If two drops of this indicator in 10 c.c. of water produce a green or more especially a yellow colour instead of the deep blue of pH 7.6, then in Cox's opinion this water is unsuitable for supply through lead pipes.

A very simple qualitative test for lead or copper is described by Fraser (1953) - "Acidify some of the water with hydrochloric acid and stir with a glass rod dipped in ammonium sulphide. Any brown colouration indicates lead or copper." The use of a second tube with distilled water and a third tube with water concentrated by boiling help in the interpretation of the phrase "any brown colouration". Sulphide methods are described by Abbott and Harris (1962) as being of low precision. Methods such as this have been known for over a hundred years and I have mentioned in the Historical Section the observation of De Mussy (1849) that a similar test failed him though the water was subsequently found to contain lead in amounts of 14 p.p.m. Iron, copper and organic matter all interfere with the function of sulphide tests. In the absence of all these, the lower limit of sensitivity is 0.1 p.p.m. (Thresh, Beale and Suckling 1958). These authors state very firmly that before any estimation of lead, an examination for iron and copper must have been made since the presence of these metals prevents any accurate estimation of the amount of lead present or may cause its presence to be entirely overlooked. They also give experimental evidence of the interfering effect of adding various proportions of iron and of copper to a solution containing 0.2 mgm. lead in 100 ml. The lowest estimation of the lead in this solution was 0.06 mgm. Since the smallest quantity of lead definitely detectable is 0.1 p.p.m. sulphide tests are of little value now that the international standards have been reduced to 0.05 p.p.m.

The Lovibond Nessleriser also uses a sulphide test and its colorimeter disc is only calibrated to 0.2 p.p.m. This apparatus has been purchased in the last few years by the Burgh Surveyors of two towns in the Scottish Borders. They appreciated the need for more frequent lead estimation from water samples

but wished to avoid the high cost of repeated specialist analyses. They had failed to appreciate that the apparatus was not sufficiently sensitive for the purpose they had in mind.

Tests such as these might be of value to the general practitioner if used in some form of crude plumbo-solvency test. If a piece of new lead sheet or lead piping was left in a sample of water for twelve hours and the sample was tested by one of these methods, a dense cloud of lead sulphide might give the practitioner a great respect for the aggressive potentialities of the water.

In Geochemical exploration, geologists use a method described by Huff (1948). The sensitivity of this test permits the detection of 0.01 p.p.m. lead and the test can be made in a few minutes in the field. This range of sensitivity would be ideal also for the general practitioner, but one of the dithizone solutions used has to be freshly prepared each day. This is no handicap to a geologist setting out from a base for a day prospecting, testing a large number of samples as he goes along. It would present great difficulties to the general practitioner who did not have good laboratory services readily available and wished to test a small number of samples. Organic matter in the water causes stable emulsions to form between the organic solvent and the water, and interferes with the test. Despite its limitations, this test could be very valuable to the general practitioner wishing to screen a large number of water samples from different parts of his practice on one day. No elaborate apparatus is required.

It can be seen that there is no completely satisfactory method available to the general practitioner to study the problem of plumbo-solvency within his own practice.

Symptoms and Signs Attributed to Lead.

Much has been written about this subject. A very clear description of the clinical types of lead poisoning is given by the Report of the Committee on Lead Poisoning of the Industrial Hygiene Section of the American Public Health Association (1943).

This report, while indicating that industrial lead poisoning as commonly seen, is to some degree a mixture of the various types, separates out for convenience and description three types - Alimentary, Neuromuscular and Encephalopathic.

The Alimentary type is by far the most frequent and is characterised by intermittent abdominal discomfort with a feeling of heaviness in the region around the umbilicus. The more severe cases show frank colic. There is usually obstinate constipation, but rarely a brief period of diarrhoea at the onset precedes this. There is usually anorexia, a bad taste in the mouth, and frequently nausea and vomiting. When there is hunger there may be a feeling of fullness after taking a little food. Lassitude and general weakness will occur and there is likely to be some arthralgia and general stiffness and aching. Dizziness and headache may also be a cause for complaint.

In the Neuromuscular type the gastro-intestinal symptoms are less disturbing. The chief complaint is of weakness or paralysis of the extensor muscle groups of the forearm and hands. Headache, vertigo and insomnia are more prominent, and joint and muscle pain and stiffness are more marked. Weakness of extensor muscles may be followed by a true paralysis.

The Encephalopathic type may show itself as sudden excitation, confusion, mania, and convulsions, followed by coma, or the picture may be less severe and

of short duration with headache, dizziness, confusion and either a troublesome insomnia or some degree of somnolence. Encephalopathy, the most serious manifestation of lead poisoning, is also the rarest except in the case of children, among whom it is the prevalent type.

As evidence of the mixing of the various types, it may be said that some degree of involvement of the gastro-intestinal tract is almost always seen and that mild cerebral symptoms occur in all types of cases.

Jones (1935), giving experience of examination of 1,500 men suspected of plumbism or on compensation for plumbism, classified the disorder according to evidence of

1) Abnormal lead absorption,
2) Incipient lead intoxication,
3) Definite lead poisoning.

This is a valuable approach for diagnostic purposes, but a striking feature of Jones' table of Common Signs and Symptoms is the vagueness of the symptomatology up to the level of incipient intoxication. Thus, suggestive evidence of abnormal lead absorption is that the patient is restive, moody, easily excited and "flustered". He has a persistent metallic taste, slight loss of appetite, slight constipation, and is irritable and unco-operative. Suggestive evidence of incipient intoxication includes pallor, jaundice, anorexia, coated tongue, slight abdominal colic, constipation, slight headache, insomnia, slight dizziness, palpitation, increased irritability and increased reflexes. There is also muscle soreness, easy fatigability and hypotension. To both these lists must be added the presence of a lead line, but Jones comments that this sign cannot be relied on as many severely poisoned persons do not show any trace of a lead line while marked lead lines are found in others who have no definite evidence of intoxication.

The need for laboratory aids in diagnosis is very obvious, but these will be discussed separately along with anaemia.

Aub, et.al. (1925) described a clinical diagnostic standard used in the pottery trade. This divides the recognised signs and symptoms into two groups: the first of major symptoms; the second of more general and less acute features. A diagnosis of lead poisoning is made with two major symptoms from different systems as well as numerous minor symptoms. If only one of the major features, such as colic or muscular incoordination, is present, then at least two of the different systems in the minor symptom group must be involved: digestive, muscular, nervous, vascular, or certain specified special organs and findings.

The criticism which Aub made of this standard which he considered a satisfactory one of its type was that it had the distinct disadvantage of attributing to a single sign or symptom a positive or negative significance. The clinical diagnosis is in fact a matter of weighing up subtle gradations in the degree of many symptoms and signs. It was, therefore, considered that in the early diagnosis of lead poisoning no fast rules could be established, and the opinion must depend on keen judgement.

Lane (1949) described the earliest symptoms as vague, the patient being moody, irritable and uncooperative. His work might fall off in quantity and quality. He may be unnaturally tired but unable to sleep. As early signs, he described pallor, tremor (occurring rarely) and lead line.

Browning (1961) gave the chief early symptoms as fatigue, disturbance of sleep and constipation.

Wolff (1958) regarded anorexia as the earliest symptom, frequently accompanied by an ill-defined intermittent abdominal pain. There might be some weight loss, the tendency to constipation develops slowly and occasionally there is alternating diarrhoea and constipation. In the nervous system, it is usual to get general weakness, headache, giddiness and also insomnia. He also mentions arthralgia, pallor and the lead line and gives criteria for suspension from lead work. The presence of vague symptoms, an increase of porphyrins in the urine, or a fall in haemoglobin he regards as signals for action. He permits return to work when the haemoglobin is 100 per cent. (14.6 g/100 c.c.) and no urinary porphyrins have been observed for two months. This usually means a change of occupation lasting four to five months, but by use of this standard he has had a reduction in lead poisoning from ten cases in two years to none in the following six years.

Johnstone (1948) has attempted to define the frequency of symptoms. In 164 cases of lead poisoning he lists 37 symptoms and signs which have been attributed to lead in the past and records the frequency with which these occurred or did not occur in his series. Twelve of these symptoms and signs were found once or not at all in the series and this group includes jaundice, which has been described by Jones as early suggestive evidence of incipient lead poisoning. The frequency of occurrence of the commonest symptoms present in 118 patients or more was in the following order: headache, pallor, weakness, anorexia, colic, nervousness, lassitude. Constipation occurred only in 102 cases, weight loss in 88, nausea in 77, vertigo in 28, vomiting in 11 and diarrhoea in 9.

Sollman (1942), giving detailed description of the effects of lead, described digestive disturbances as being among the earliest and most common phenomena.

They begin with mild stomatitis, foul breath, sweet metallic taste, anorexia and nausea. Diarrhoea is frequent in the early stages; later there is usually very obstinate constipation, or the two may alternate. The abdomen may be tender. These effects are based partly on mild inflammation of the whole alimentary tract, which later on is complicated by the colic. Chronic parotitis sometimes occurs, perhaps as a part of the stomatitis. The description of lead colic is of acute attacks of paroxysms of intense pain, radiating from the umbilicus and relieved by pressure. The patient, therefore, retracts his abdominal muscles or may lie pressing his fists against the painful region. The pulse is often slowed, sometimes to 40 or 50 per minute. Nausea and vomiting are frequent. Entirely analogous effects may be produced in animals except that with these diarrhoea may be more common than constipation.

Leschke (1934) described the abdominal pains as preceded by a feeling of fullness in the stomach and a lack of appetite, due to gastritis, which is detectable gastroscopically or by X-rays, and may lead to ulceration. He described the pains in lead colic as being mostly localised below the umbilicus and often in the region of the appendix. Spastic constipation occurs in about 85 per cent. of the cases and only in about 15 per cent. is there diarrhoea due to enteritis. Legge and Goadby (1912) also describe 15 per cent. of cases of lead colic as suffering from intermittent diarrhoea. Leschke also discusses vascular spasm as an effect of lead poisoning producing effects ranging from paleness of skin to angina pectoris and able to be observed directly in the conjuctival and retinal vessels.

The symptoms are, therefore, of extreme vagueness in the early stages in contrast to the more

advanced features which should be much simpler to diagnose in industry, but while industrial action can be taken to reduce exposure on such vague symptomatology this presents a well-nigh impossible diagnostic problem in general practice because it can be imitated by so many other conditions. While constipation is a prominent feature of industrial poisoning, diarrhoea has also been recorded in a smaller proportion of cases. It should be noted, however, that there are in the literature other comments attributing effects to lead which are even more vague than those which have been mentioned.

Minot (1938) discussed the difficulty in recognising the harm done by small amounts of lead absorbed by the average individual. In view of the evidence of the effects of lead in great dilution on isolated tissues, the continuous absorption of any amount must result in less than optimal conditions for the organism as a whole. At that time, Minot considered that we did not know what to look for as manifestations of this slightly unfavourable condition. It seemed doubtful that the usual recognised signs and symptoms of plumbism were to be expected in more than an occasional highly susceptible person. She therefore regarded it as important to establish a more delicate set of criteria for the recognition of early slight injury from lead.

In a preface to "Lead in Food" MacNalty (1938) commented that the harmful effects of continued small doses of lead begin from the moment the lead is absorbed and that the crude symptom complex of chronic poisoning is merely the final stage of a long series of more subtle metabolic disturbances which elude our imperfect methods of detection. He suggested that "there is no threshold below which still smaller doses can be regarded as being without some adverse effect". Complete absence of lead in food was therefore the ideal.

Ashe (1943) discussing the symptoms and signs of thirty proved cases of plumbism stressed the most striking fact that in many instances physical signs were conspicuous by their absence.

Porritt (1931) divided plumbism into two types - classical lead poisoning, with colic, wrist drop, blue line on the gums and anaemia, and an altogether different group of symptoms produced by "infinitesimal doses of lead extending over a long period of time". The symptoms he described, however, seem to be a more detailed account of those associated by Jones with increased lead absorption.

Milligan (1931) agreeing that mild insidious forms of plumbism often escape notice listed a number of conditions which he believed to be due to the taking of minute quantities of lead. This includes abortion, premature birth, marasmus and infantile convulsions, neuritis, mental depression, epileptiform convulsions in adults, diarrhoea, constipation, and severe anaemia followed by death. These observations are from a number of years of study of the effects of water supplies with unusually high lead contents.

Williams (1939) described a multiple neuritis affecting sensory nerves with no motor disturbance.

Bramwell (1931) and also Picard (1934) described cases in which the diagnosis of plumbism was made with difficulty, because other diseases were simulated. More recently, Mann (1962), showed how of 25 cases of lead poisoning, presenting with acute abdominal symptoms, six had an unnecessary laparotomy but he believed that these cases would fall within the textbook diagnosis of lead poisoning if this had been considered.

Bagchi (1941) has also been impressed with an insidious type of illness occurring among Hindu women and children and suggests as its cause the application to the skin of cheap vermilion which contains red lead mixed with a red synthetic dye.

Ingleson (1934) gives a number of opinions that lead poisoning from a water supply gives rise to symptoms which are not typical of those observed in occupational cases. Unless there is some other reason to suspect plumbism it is quite easy to overlook their true cause.

One interesting observation on this point is that the Medical Officer of Health for Sheffield (White, 1886), observed that at the time of an outbreak of plumbism from water supplies, the disease was not infrequent in the City in certain workers, for example, file-makers, and that local doctors, though very familiar with occupational plumbism, did not until after the scare report on the presence of plumbism from the water supplies.

In paediatric cases, the symptom of pica (Shrand 1961) is found in a high proportion of children suffering from plumbism, and a much smaller proportion show bands of increased density on radiographs at the ends of long bones. Most of the other features are similar to those which have already been described with a marked tendency towards development of encephalopathy which is frequently followed by permanent mental sequelae.

The search for other manifestations of plumbism in children has produced the evidence that 45 per cent. of a series of 122 children with mental retardation or severe behaviour disorders, showed a blood lead level which was considered to be outside the normal range (Moncrieff, Koumides, Clayton, Patrick, Renwick and Roberts (1964)).

Laboratory Methods for the Diagnosis of Lead Poisoning.

Punctate Basophilia.

Lane (1949) described the results of the numerous investigations on this subject as so contradictory that the literature was in a state of chaos. He supported this with a table giving the danger levels suggested by various authorities from 1919 to 1940, ranging from 100 punctate basophil cells per million red cells to 3,000 punctate basophil cells per million red cells. He considered some of this disagreement to be due to variations in methods used, and some to attributing to punctate basophilia an undeserved specificity and accuracy. In the Millroy Lectures, Lane quoted his own opinion in 1931 that the danger level was 3,000 punctate basophil cells per million red cells. The dark ground method which he uses gives results considerably higher than those obtained when transmitted light is used, and this is quoted as approximately twice as great. He states that punctate basophilia varying between one and three thousand per million has been observed in 8 per cent. of normal individuals with films examined by this method and later indicates that one to five thousand punctate basophils per million red blood cells are likely to be present in the minor degrees of lead absorption with an absence of signs and symptoms of poisoning and would appear to be consistent with good health. The same writer, in 1964, describes punctate basophil counts in a healthy lead worker showing evidence of increased lead absorption as being less than 10,000 per million red cells. High lead absorption, in which workers are exposed to danger, is associated with a punctate basophil count ranging from five to twenty thousand per million red blood cells.

Browning (1961) states that most observers now consider anything above ten thousand punctate basophil cells per million (dark ground method) a danger signal and an indication for suspension from work, even if unaccompanied by symptoms and physical signs, but Hunter (1957) gives the danger level of three thousand stippled cells per million erythrocytes by dark ground illumination.

The detailed observations of the Committee on Lead Poisoning of the Industrial Hygiene Section of the American Public Health Association (1943) are very valuable. Basophilic granules of varying size can normally be demonstrated in human red blood corpuscles. There is a wide variation in the number of these in response to a variety of environmental factors. Lead absorption above certain levels is well known to result in an increase in these "stippled" red cells.

While the lack of specificity, the wide range of individual variation and the variability of results obtained by different observers is a handicap the method is very useful when properly controlled and interpreted. The basic requirements are the making of blood films which give a single layer of erythrocytes and allow each one to be examined. Various methods of staining have been used successfully. Sufficient time must be allowed to examine each erythrocyte in each field and to count the "stippled" erythrocytes in not less than 50 fields, using an oil immersion lens which will give sharp definition at a magnification of not less than 900 diameters. The useful comment is made that the type of microscope which is commonly available for routine work in clinical laboratories does not give sharp enough definition to yield satisfactory results even in the hands of a skilled microscopist. The chief factors of accuracy are satisfactory microscopic equipment, uniform films and patience in examining these.

Uneven films and thick smears are valueless and hurried examination of films will give misleading results. This Committee considered that, in general, only a small percentage of normal blood films would show more than 1,000 punctate basophil cells per million red cells, and the large proportion of the counts would be considerably below this figure. Average or mean normal numbers are approximately 300 to 350 per million erythrocytes if the method of staining is sensitive and the technique of examination is carefully carried out.

In the supervision of workers in industry, this microscopic examination of the blood is useful in determining whether the general lead exposure is within safe limits. Usually some conservative and more or less arbitrary limit is set as representing the upper permissible limit and with punctate basophilia this is commonly regarded as 800 to 1,000 stippled cells per million erythrocytes. The occurrence of findings above this limit in the opinion of this American committee is the signal for the transfer of individuals to less exposed jobs and for a re-examination of the source of exposure to determine whether or not some new factor has developed.

In the observations which will be recorded subsequently counts of less than 1,000 basophil cells per million red blood cells have not been reported in detail but as "less than 0.1 per cent.". These counts were done personally by a consultant pathologist whose assistance in this part of the research study was greatly valued. The microscopic apparatus was more than adequate (magnification 1,300 diameters). Films were stained with methylene blue and were examined by transmitted light. Any film which proved too thick for satisfactory examination was rejected.

Apart from exposure to lead the other most notable conditions in which punctate basophilia occurs are (according to Lane): Pernicious Anaemia, the Leukemias, and Cachexia following neoplasm.

Lead in Blood.

Cumings (1963) listed twenty-one references to Encephalopathy from inorganic lead intoxication with a very wide variation in the figures quoted for blood lead level, ranging from 28 µg/100 ml. to 880 µg/100 ml. There was very little correlation between the level of blood lead and the degree of lead intoxication.

Lane (1949) stated that there was no justification for claims of critical values of lead in the blood above which poisoning occurred and below which safety might be presumed. Hunter (1957) agreed with this, because sometimes in a case of chronic plumbism, the blood lead repeatedly shows normal figures (0.03 to 0.08 mg/100 ml.) whereas occasionally a healthy lead worker shows high results. In 1964 Lane included in the group of features associated with dangerously high lead absorption, a blood lead level above 0.08 mg./100 ml.

The report of the American Public Health Association Committee on Lead Poisoning (1943) gives the concentration of lead in the blood of normal North Americans, with no occupational lead exposure, as ranging from 0.01 to 0.06 mgm./100 g. of whole blood. Values in excess of 0.05 mgm. are rare in normal individuals and most of the results are between 0.01 and 0.04 mgm. with a mean value slightly under 0.03 mgm. The upper limit of safe lead concentration in the blood of regularly exposed industrial workmen has not been defined with the necessary degree of precision according to this report, which considers that the upper limit of safety for the concentration of lead in the blood

lies somewhere between 0.05 and 0.07 mgm./100 g. and is probably not far from the latter figure.

Kehoe (1961) gives a mean value for normal blood lead as 0.03 mgm./100 gm. As already mentioned (p.23), he states very dogmatically that in his experience, no case of even the mildest form of poisoning has been induced by the absorption of inorganic compounds of lead with a blood lead level below approximately 0.08 mgm./100 g. of whole blood. This is a very definite statement which does not agree with other writers on the subject. It follows a table demonstrating the association of blood lead levels with the order of severity of exposure to lead in industrial conditions. Of 75 men subject to "very severe, very dangerous, lead exposure", nine are tabulated in the 0.04 - 0.059 mgm./100 g. category and a further twelve in the 0.06 - 0.079 mgm./100 g. level. The remaining 54 men in this group had blood lead levels in excess of 0.08 mgm./100 g.

While these figures refer to males working in industry, paediatric studies have concentrated on a much lower level of toxicity.

Moncrieff, et.al. (1964) give 36 µg/100 ml. as the upper limit of normal for children. They demonstrate the dramatic effects of free availability of blood lead estimation in the Hospital for Sick Children, Great Ormond Street, London.

Twelve patients with lead poisoning were diagnosed in a ten year period, but when blood lead estimations became freely available a total of thirty-seven children were found having blood lead levels above 50 µg./100 ml. in a space of two years and four months, and a further forty-two children had blood lead levels in the range 40 to 50 µg./100 ml. which they considered to be outside the limits of normal.

These authors consider that preconceived ideas about the level of blood lead at which toxicity occurs should be abandoned and that levels of lead in blood between 40 and 60 µg./100 ml. should be carefully considered in the light of the clinical findings in children.

Urine Lead Estimation.

This is preferred in industry to blood lead estimation, partly because of the obvious dislike of the workers for repeated venipuncture. Single urine samples are used for these estimations and though these as a rule prove satisfactory, a 24-hour urine collection is obviously better. For the most part in these studies, blood lead estimations have been used in an attempt to obtain greater accuracy, but a certain number of 24-hour urine samples have also been obtained.

Lane (1964) indicates that a healthy worker with increased lead absorption will have a urinary lead level below 150 µg./litre where a lead worker with dangerously high lead absorption will have a urinary lead excretion in excess of 200 µg./litre.

Difficulties associated with Lead Analyses.

These are notorious and very justly so. Lead is so frequently used that accidental contamination of the sample must be guarded against at all stages. Stainless steel needles and plastic syringes were used for the collection of blood samples in our studies, because one well known source of contamination is the solder joint of a glass and metal syringe and even the solder joint at the base of some types of needle has been noted as a possible cause of contamination. Glass laboratory containers were used for human blood samples but the blood samples obtained from dogs by the veterinary surgeons were taken from stainless steel

needles direct into small polythene bottles supplied by the laboratory without the use of a syringe. For 24-hour samples acid washed one litre polythene containers were used. Samples of milk were submitted to the laboratories in specially prepared polythene containers or in the original cartons if this was possible. The foodstuffs were sent to the laboratory either in their original packages or in domestic polythene food storage bags. Water samples were collected only into containers provided by the water analyst.

The staff of the laboratory at Peel Hospital, who did a large number of analyses for this study were acutely aware of the possibilities of contamination. Only lead free chemicals or chemicals prepared for lead analysis were used. The glassware was specially prepared for the purpose. The original method used consisted of the dry ashing of samples in a muffled furnace at 450°C. as described by Tompsett and Anderson (1935), but though this is a standard method and was done with the best skill and care available by a senior technician who had used it previously, there was so much dissatisfaction with ability to reproduce results that this part of the method was abandoned and a wet ashing method, described by Varley (1958), was substituted. Both methods used a Dithizone extraction for the lead after ashing. It was noted latterly that Kehoe makes specific mention that parallel analyses of urine samples are not readily applicable to lead estimation. The division of a specimen is fraught with gross possibilities of error, since even after slight cooling, the precipitation of phosphates, for example, may cause the sample to be no longer homogeneous.

Observations of the difficulties of lead analyses were not confined to this laboratory however. A water sample on one occasion was collected in a container whose stopper was considered not to be sufficiently watertight to stand the journey to the laboratory. As there was no other container of that size available, the sample was decanted into two smaller containers. The water analyst was well aware that these two containers represented the same sample and all three bottles had been provided by his laboratory for lead estimation purposes. The laboratory checked the results four times and annotated the report form that they had done so, but the results of the two bottles were reported as 1.63 p.p.m. and 0.802 p.p.m. The original sample contained no sediment obvious to the naked eye, but the damaged stopper would prevent it being shaken up before the division was made. A veterinary surgeon in Devon (McKellar 1964) has a similar example of two blood sample bottles filled from the same syringe and reported by an internationally famous veterinary laboratory, which has done much research in trace elements (Ministry of Agriculture Laboratory, Weybridge), as having widely different lead contents in the two bottles (0.5 p.p.m. and $<$ 0.3 p.p.m.). A series of milk samples analysed at the Royal (Dick) Veterinary College immediately after the department concerned had moved to a new laboratory gave a highly improbable series of results for a normal control group of cattle belonging to the College. Copper analyses being done at the same time in that department for a research study, also showed temporarily gross aberrations. These remarks are in no way intended to be disparaging to the laboratories concerned. The help which they have so freely given is fully appreciated and all the more so because of these evidences of the difficulties with which they have had to contend.

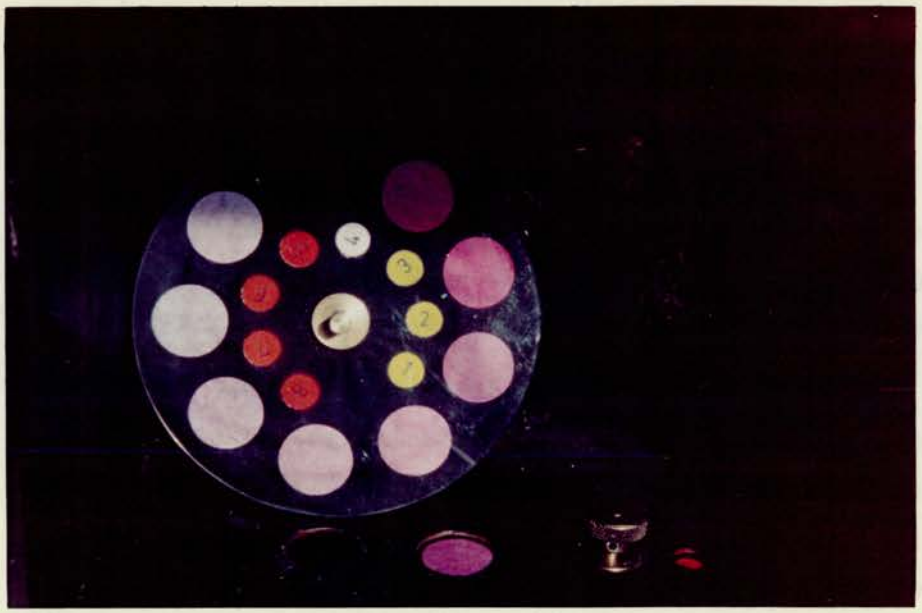


Plate 6.

Fluorescent colorimeter disc of Donath apparatus. A new disc is being compared with the original one in the apparatus after 2000 tests.

Plate 7.

The apparatus required for the Donath test: pipette, extraction solution, test-tubes and Donath's fluorescence comparator.

Facing page 54.

Urine Coproporphyrin Estimation.

The development of this as a method for the supervision of workers in lead-using industries has been described in the historical section, where it was shown that this is an established, useful and sensitive test.

In 1956, Donath described a simple portable apparatus for use by the industrial physician screening an industrial population exposed to lead. His method is essentially a comparison of the fluorescent colour of the porphyrin content of a sample of urine as developed after extraction with ether and glacial acetic acid, with that of a series of paper strips of graded degree of fluorescence. This apparatus which has been used extensively in the present studies will be described in some detail. It is available commercially in Holland at a price of £30 or the plans and fluorescent scale may be purchased and the apparatus constructed elsewhere.

The Fluorescent Scale. This is made from varying concentrations of Rhodamine B. (the hydrochloride of tetra-ethyl-diamin-ortho-carboxyphenyl-xanthyllium). The fluorescent colours are arranged on a disc which rotates in the apparatus and are calibrated according to degrees of fluorescence. Plate 6 shows the fluorescence of a new disc being compared with one which had been in use for some 2,000 tests. The apparatus contains a Philips ultra-violet analysis lamp (H.P.". 125 W.) and there is a Philips 58205 ch/03 choke in the base. The complete apparatus and equipment is shown in Plate 7 . The equipment consists of a 10 c.c. pipette, test tubes of pyrex (to minimise fluorescence from the glass) and a solution of 90 per cent. technical ether and 10 per cent. glacial acetic acid.

Method. 2 c.c. of the ether/acetic acid extraction solution is added to 10 c.c. of urine in a test tube. The tube is stoppered and shaken vigorously three times and the stopper carefully removed. This suffices to leave the coproporphyrin in a foamy layer of ether on the surface of the urine. The test tube is pressed into an aperture on the surface of the apparatus below the ultra-violet lamp and exposed to the ultra-violet light for at least ten minutes. If the test tube is shaken too long an emulsion may be created and the coproporphyrin will not be collected in the foamy layer of the ether. If the cork is removed too suddenly, there may be excessive frothing which will spread the coproporphyrin up the sides of the test tube. After the ten minute interval the fluorescent colour of the ether layer is compared with the fluorescence of the colour scale, and the appropriate degree of the calibration noted. This should be done in a darkened room and the test tube should be pressed far enough into the apparatus so that only the ether layer is visible or the fluorescence of the urine itself may prove distracting. Clips are provided on the back of the apparatus so that four samples may be exposed to ultra-violet radiation at the same time. Using a fluorometer, Donath calibrated his apparatus with pure coproporphyrin with the following degrees of fluorescence.

Degree of Fluorescence	Concentration in µg./litre of coproporphyrin
1	0 - 50
2	50 - 100
3	100 - 200
4	200 - 400
5	400 - 800
6	800 - 1600
7	1600 - 3000
8	3000 - 5000

Donath claimed that the apparatus yields reliably reproducible results with a negligible variability due to observer error. He considered that degree 4 (200-400 µg./litre) was suspicious and that values below that were to be considered non-pathological in industry though he quotes three references giving normal values not higher than 100 µg./litre.

Zielhuis (1961) has also used this apparatus in industrial work in Holland. He found it to be a valuable tool in the prevention of inorganic lead intoxication. He calculated average results for groups of workers and found that, if the average for such a group exceeded 1.5 degrees on the Donath scale, there was an increase of lead intake above normal. An average of 2 to 2.5 was the maximum allowable level for groups of workers and if the average exceeded 2.5 degrees, the maximum allowable concentration for lead in air (0.1 mg.Pb./per cu.m.) had probably been surpassed.

Zielhuis (1962) also found that in individual investigations, a repeated coproporphyrin excretion below 3 degrees on the Donath scale indicates that no harmful uptake of inorganic lead exists. A result of 3 on the Donath scale may be found in 10 per cent. of normal occupationally non-exposed male workers or in workers who definitely are poisoned as shown by a lowered haemoglobin and increased punctate basophilia. Degree 3, therefore, does not discriminate between "normal" and "poisoning" in an individual. However, in a group of workers the significance of degree 3 may be interpreted in regard to the coproporphyrin excretion of the group as such. The rise in coproporphyrin is a very early sign of increased inorganic lead uptake. It generally rises quickly to a high level above degree 3, but as it is too sensitive a criterion, one cannot deduce the extent of poisoning

from the individual values. An increased coproporhyrin excretion (greater than 3) in an individual, therefore, indicates that this individual has an increased uptake but does not indicate the level of increased uptake. These observations are all based upon studies of industrial workers. In occupationally non-exposed male workers 70 per cent. gave a Donath reading of 1 (0-50 µg./litre), 20 per cent degree 2 (50-100 µg./litre) and 10 per cent degree 3 (100-200 µg./litre).

There have been many different opinions on the upper limit of normal for urine coproporphyrin excretion. Extractions of coproporphyrin from ether into hydrochloric acid and mobilisation of coproporphyrin precursors with iodine have been recommended (Benson and Chisholm, 1960). These more complicated procedures detract considerably from the advantage of allowing the unaided single handed practitioner to screen a large number of samples rapidly and so the method described by Donath has been followed. One modification suggested by Zielhuis was that degree 8 on the Donath scale was very difficult to identify in comparison with degree 7, because of the intensity of the fluorescence. He therefore suggested that degree 7 should be regarded as coproporphyrinuria in excess of 1600 µg./litre. Only one of my patients has reached this level but I would agree that interpretation of the scale at this level is very difficult indeed.

With regard to normal values Vanotti makes the comment - "The values deduced from coproporphyrin elimination in the urine of a normal person vary according to the methods used and the workers computing them. It can, however, be assumed from the best observations that the daily urinary elimination of coproporphyrin varies between 0 and 100 µg."

Where the sensitivity of the test is concerned the observation of Lane (1964) is noteworthy - "For most trades with substantial lead hazard the coproporphyrin test is too sensitive". A test which is too sensitive for a substantial lead hazard would appear to be particularly suitable for lesser degrees of non-industrial exposure. Since part of these studies involves the supervision of maternity patients this great sensitivity is most valuable.

From this description of the methods of study available and the preceding notes on the history of lead poisoning some of the difficulties of early diagnosis are evident. When a whole community is drinking water which at times is known to contain lead in small quantities, it is necessary to identify the earliest features of harm which can reasonably be attributed to that metal. However, a clear and concise definition of what constitutes a minimum standard for "lead poisoning" is hard to find.

An enquiry to H.M. Medical Inspector of Factories revealed that there was no firm legal standard for the diagnosis of industrial lead poisoning (Doig 1965). A definition of lead intoxication given by Goldberg (1964) consists of a blood lead level higher than the normal range for the laboratory concerned in association with evidence of disturbance of porphyrin metabolism. While this is a useful definition of the early features of upset in the functioning of the body based on laboratory findings, it would not satisfy some experts on the subject such as Kehoe, for example. Zielhuis (1961B) demonstrates the problem very neatly by defining three degrees of lead poisoning. The first of these is the earliest sign of physiological variation in the body's function,

the second is the level at which industrial action is required to reduce or avoid further exposure, and the third is that degree of poisoning which requires the stopping of work and for which compensation will be paid. In the studies which follow, with the exception of the very small group of industrial cases, it is the first of these categories with which we are concerned.

From the information which has been given it can be seen that the symptoms may be so vague as to be of little value in general practice. It would be impossible to differentiate them from the early symptoms of many other conditions. When it is realised that physical signs might also be absent the difficulties with the problem become manifest. Of the laboratory tests available, blood lead estimation is elaborate and difficult and is not suitable for screening any large number of patients because of the size of the sample of blood required and the laboratory difficulties involved. Estimation of urine coproporphyrin is a sensitive but simple test but is not specific for lead. Punctate basophilia is less sensitive but more specific. It can be fairly said, therefore, that all the methods available for the study of this problem have disadvantages associated with them.

SECTION III

The Sources of Lead Intake

Plate 8.

Glenmead filter from above - after improvements.

Plate 9.

Glenbenna filter - after improvements.

The Water Supplies.

Innerleithen and Walkerburn have water catchment areas on the hills on opposide sides of the River Tweed. The greater part of the practice is supplied by Innerleithen Burgh Water Supply.

History of Innerleithen Water Supply.

The water supply dates from 1877 and is very simple in type. The gathering ground consists of some 2,000 acres lying in the hills to the south-east of Walkerburn on the opposide side of the River Tweed from the Burgh. The water is derived from the two tributaries of the Bold Burn. The original scheme made use of Glen Mead Burn only and water was conveyed to Innerleithen by a six inch iron main, but this original 1877 scheme proved inadequate by 1900 and an additional supply was drawn from the Glenbenna Burn with an extra five inch main to the town. There is neither storage reservoir nor chlorination of these supplies. The water is collected in tanks with a total capacity of 90,000 gallons, which is rather less than half a day's requirement for the Burgh.

In 1931, there were great difficulties in the supply of water to the higher parts of the town. The Town Council obtained consultant advice on the problem and was advised to abandon the Bold Burn completely and build a new water works on the Fingland Burn. This had a very much bigger flow than the Bold Burn and it would be possible, if desired, to provide a reservoir with a capacity of about 70 million gallons without much difficulty, whereas an attempt to construct a reservoir on the Bold Burn would have been a vast undertaking. The estimated cost of the Fingland Scheme in 1931 was £7,160 excluding the cost

Plate 10.

Innerleithen water storage: The tank extends from the hut to the edge of the grass covered mound on the left.

Facing page 61.

of a reservoir, but the Town Council took no further action at that time.

In 1949, interest in this project was revised and a meeting was held between representatives of the Town Council, the County Council, and the Department of Health, to consider a regional water scheme for the Burgh of Innerleithen, the village of Walkerburn, and the rural area of Traquair through which a water supply from the Fingland Burn would pass. The estimated cost of the scheme was now £18,300 and it was not considered necessary by the County Council and the Department of Health for Scotland. Criticism was levelled at the high water consumption in Innerleithen Burgh and it was suggested that in view of the age of the distribution mains their renewal should be given first priority.

By 1956, the Town Council had relaid practically the whole of the mains in the older part of the Burgh. The problem was then reviewed once again by another firm of consulting engineers. Their report gives a quantity of 210,000 gallons per day as being supplied to the town except during periods of unusual drought. They commented on the considerable encrustation which must have taken place in the six inch diameter main of 1877 and the five inch pipe laid in 1900. About half of the total length had been cleaned in 1948 but not thoroughly descaled by boring. Of the two filters which were housed near the town they considered that the one installed in 1900 could be disregarded and the other, a Bells filter installed in 1927, was acting merely as a coarse strainer. The filter charge had been replaced by coarse stone and the makers stated that it would be impossible for the filter arms to rotate with such a filtering medium inside it. Three such filters in good working order would be required to deal with 210,000 gallons per day

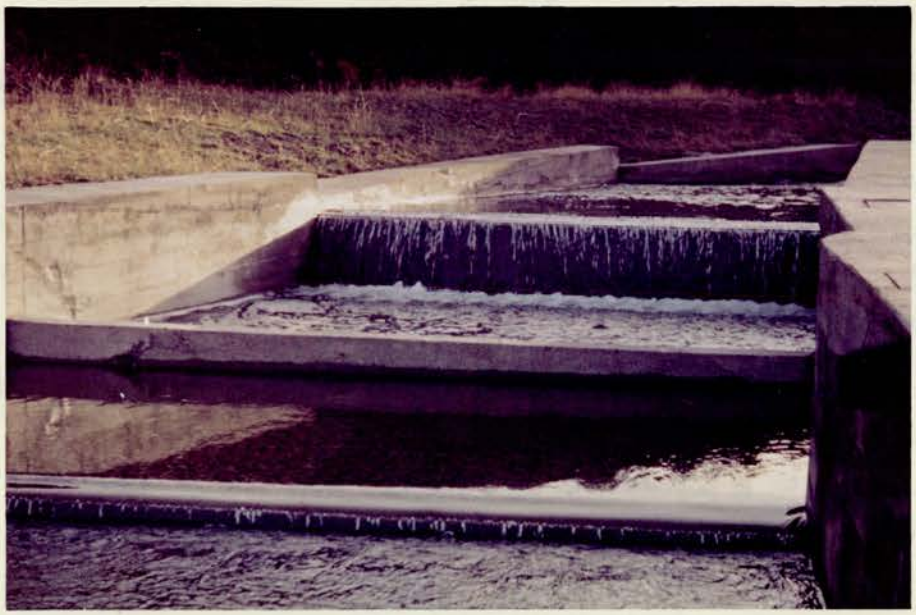


Plate 11.

Glenmead filter showing water running out of settling basin and down through first filter, up through second and over and down through third filter bed.

Plate 12.

Bypass valve in the burn outside Glenmead filter.

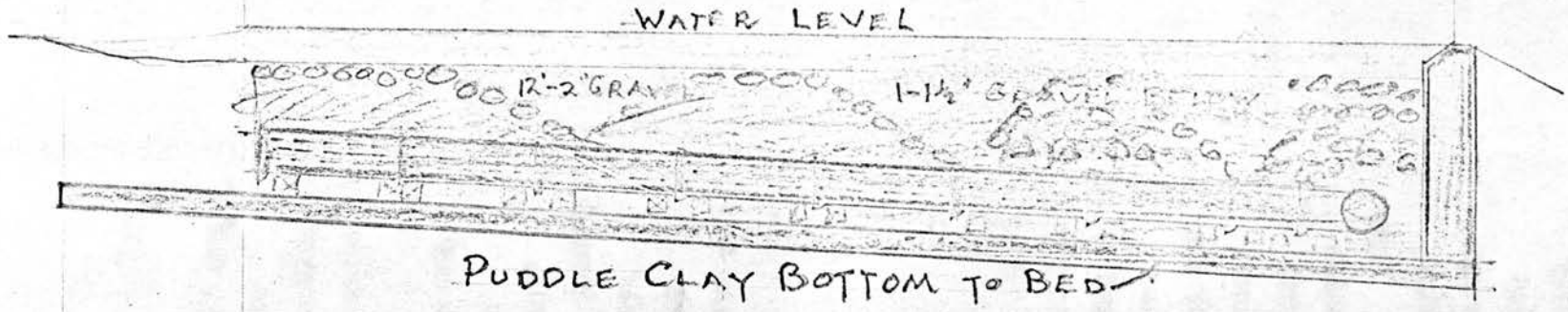
in an adequate fashion. The consultants' recommendations were for an immediate expenditure of £4,800 to renovate and improve the existing supply and thereafter extensive investigations for a future more permanent scheme. The Town Council again took no action of these recommendations.

On considering these estimates for improvements and extensions to water supplies it should be realised that with a population of only 2,300 the total Town Council annual expenditure amounts to some £25,000 and this is met by a Burgh rate of twenty-one shillings per pound. (This does not include the County Council levy or certain Government Grants which partly offset that levy.) It had, however, been ascertained that the Burgh did not fall within the provisions of the Rural Water Supplies and Sewage Act,1944, which made grants available for water and drainage projects. It can, therefore, be seen that the adoption of the Fingland Scheme for a new water supply and the abandoning of the old one would have led to an enormous increase in the Rates of the town and the preoccupation was more with the supply available to a few houses in the upper part of the town rather than to defects in water quality, which received little mention in these reports.

By 1959, the catchment area had been purchased by the Forestry Commission and was completely planted. It had previously been uncultivated. The area was entirely enclosed by Forestry fences to keep out sheep and other animals. On one occasion only, I found that about a score of sheep were grazing inside the fences close to a small burn. There are no restrictions on walkers in the area, but these are very infrequent. There are, however, no notices to warn casual visitors that the area is the catchment for a public water supply.

Figure 3.

INNERLEITHEN WATER SUPPLY

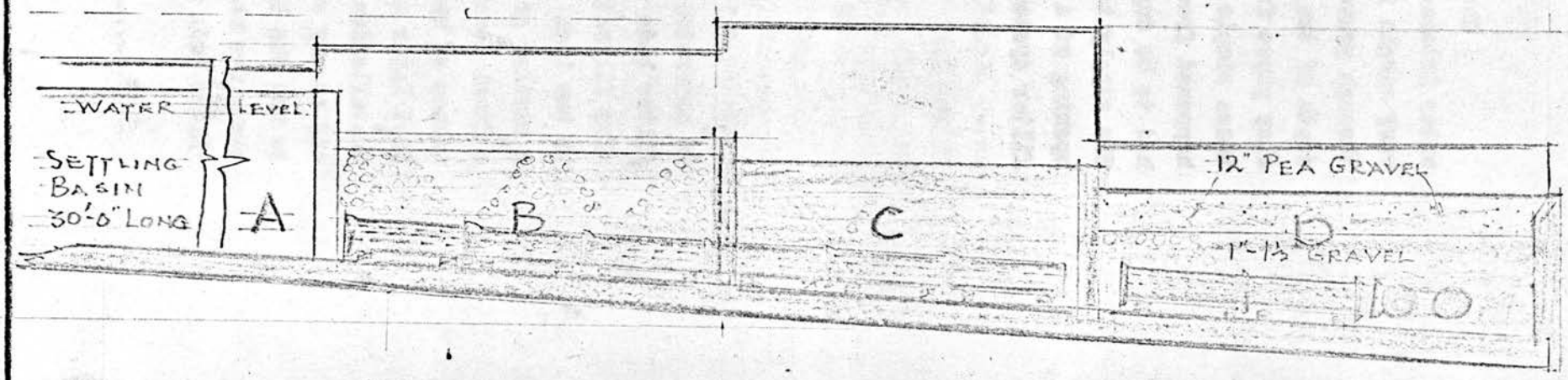


ORIGINAL FILTER BED

PUDDLE CLAY BOTTOM.
10" PERFORATED FIRECLAY PIPES SET ON BRICKS
1"-2" GRAVEL : AVERAGE DEPTH 2'-0"
PURELY DOWNWARD FLOW FILTRATION

NEW FILTER BEDS

A: SETTLING BASIN.
B: DOWNWARD FLOW FILTRATION THROUGH 2'-0" OF 1½"-2" GRAVEL.
C: UPWARD FLOW FILTRATION THROUGH 2'-0" OF 1½"-2" GRAVEL.
D: DOWNWARD FLOW FILTRATION THROUGH 18"-1"-1½" GRAVEL & 1'-0" PEA GRAVEL



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The filtration systems immediately below the water intakes on each of the two burns were formerly very simple indeed (see Fig. 3). The water passed through gravel (one inch to two inches) of an average depth of two feet by gravity flow to perforated fire-clay pipes from which it was drawn to the tanks. When these simple filters became choked with debris, which happened frequently after heavy rainfall, the gravel had to be dug out with pick and shovel, and replaced. The supply to the town was maintained, however, by the opening of a by-pass valve in the burn outside the filter system, which delivered unfiltered, untreated water directly from the burn to the main pipes leading to the town (Plate 12). This by-pass was also used if any repairs or cleaning were needed in the tanks.

In 1959-60, improvements were made to this simple gravity filtration system at the cost of approximately £1,000. Instead of the original clay bottomed filter, the whole construction was carried out in concrete. A settling basin and three separate filter beds were made. There was first downward flow filtration, through two feet of one and a half to two inch gravel, then upward flow filtration through a similar gravel bed, and after passing over a weir, a final downward flow filtration through eighteen inches of one to one and a half inch gravel and a one foot layer of pea gravel (see Plates 8,11). The installation was designed so that water could be drawn off at any stage of filtration, thus avoiding the need to use the by-pass. The layout also provided the means for using mechanical excavators for emptying the filter beds when these became clogged. In the smaller of the two filtration systems on Glenbenna Burn a metal filter plate was also installed (Plate 9).

Plate 13.

Glenbenna filters showing water running across the top of all filter beds after heavy rainfall.

Cement washed away from metal plate at final filter leaving gaps in filter.

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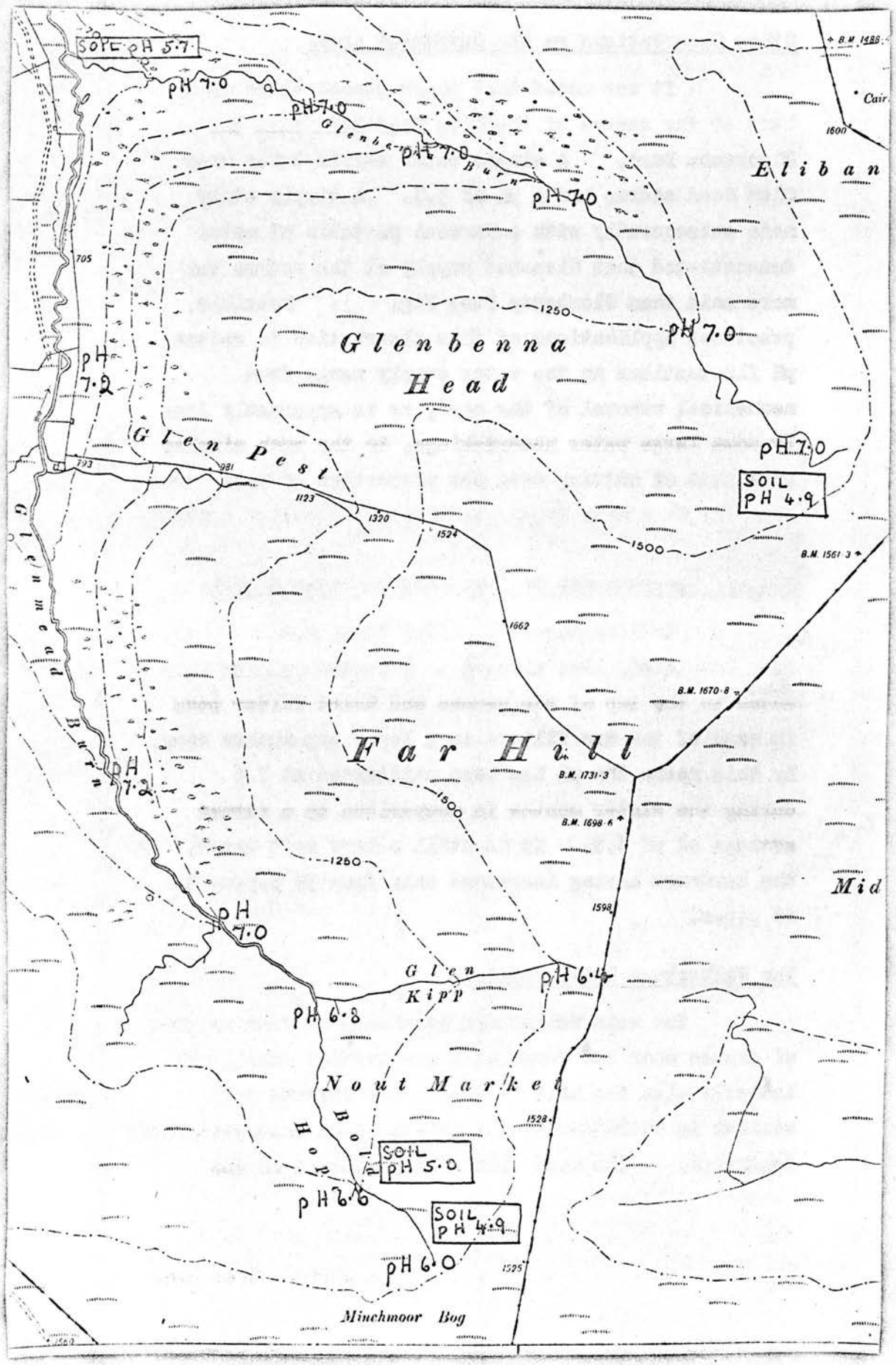
Defects in the Water Supply System.

The use of a by-pass system to supply untreated water direct to the consumer is to be deplored. In December 1959, at the time of one of the outbreaks of gastro-enteritis in the town it was disclosed that the by-pass was being used, because as a result of corrosion, the ballcock in the main tank had to be replaced. Bacteriological and chemical analyses taken specially at the time from two of the houses affected by the gastro-enteritis, were reported as satisfactory. The pH was recorded as 6.8.

With a single system of filters and tanks a by-pass system is inevitable, because periodic cleaning and repairs are required. Though the Innerleithen system had two sets of filters on two separate burns the supply from one was so much smaller than the other that no attempt was made to cut off one filter system only when cleaning was needed. A major defect of this type of filter is that, with a large volume of water after heavy rain, the water can sweep over all the weirs and only go through the last filter bed. This is shown clearly in Plate 13 . Gates are fitted to control the flow of water, but these are not always adequate. It will be noted also that in Plate 14 the cement joining the metal filter plate to the wall of the filter has been washed away leaving obvious gaps.

The report of the Ministry of Health Central Advisory Water Committee (1948) states that where the storage period is reduced to less than a month during times of drought, pre-chlorination is recommended as an additional protective measures. The Innerleithen supply lacks both storage and chlorination.

Figure 4.



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Other Observations on the Catchment Area.

It was noted that there seemed to be more peat at the source of the Glen Mead Burn than the Glenbenna Burn. A single water sample taken near Glen Mead source had a pH of 5.7. A simple study made subsequently with a Marconi portable pH meter demonstrated that Glenmead supply at the source was more acid than Glenbenna (see Fig. 4). Possible practical applications of this observation to reduce pH fluctuations in the water supply range from mechanical removal of the peat, as is apparently done by some large water undertakings, to the much simpler expedient of cutting down the proportion of water used from the Glen Mead supply at time of excessive rainfall.

Further Improvements to Innerleithen Water Supply.

In November 1964, after these studies had been completed, lime chips $\frac{3}{8}$ to $\frac{3}{4}$ inches in size were added to the top of the second and third filter beds in each of the two filters in a layer six inches deep. By this means the pH has been maintained at 7.6 during the winter months in comparison to a former average of pH 6.8. It is still a very soft water, the hardness having increased only from 39 p.p.m. to 48 p.p.m.

The Walkerburn Water Supply.

The main Walkerburn catchment is from an area of grouse moor and rough hill grazing for sheep, and latterly also for hill cattle. The filters were similar in character to the Innerleithen ones previously described. The most outstanding feature of the history of this supply is that in 1951 the water in the village developed an extremely unpleasant taste. This was easily traced to a concrete sheep dipper tank some distance above the water intake which had leaked

Plate 15.

The unpleasant appearance of Walkerburn water at the time of an epidemic. This also shows the amount of sediment in a bottle of water.

Plate 16.

Walkerburn Filter Plant - December 1962.

into the stream. A sample of water was found to contain Arsenic in a concentration of 20 p.p.m. This was, of course, speedily rectified.

The Walkerburn water became discoloured after rain and in the lowest parts of the village a large amount of unpleasant looking brown sediment appeared in the water if the tap was turned on with much force of water flow. In May 1959, at a time when this discolouration was very obvious (see Plate 15) an epidemic of diarrhoea and vomiting occurred. One hundred and sixty-two cases were known to the two practices serving the village. The outbreak was sudden, very short (almost all within 72 hours), and limited to persons on one water supply. Those people who lived in two rows of cottages served by a different water supply at the upper end of the village did not appear to be affected and I was not able to trace any spread of the illness to the surrounding countryside. I understand that one patient of the other practice went to live with friends outside the district and they subsequently developed diarrhoea and vomiting.

Reference is made to this outbreak in the Annual Report by the Medical Officer of Health and County Sanitary Inspector (1959):

> "On the face of the evidence at their disposal, the (local) doctors were inclined to suspect the water supply and accordingly bacteriological and chemical examinations were made of the supply in question - that from Priesthope on the Walker Burn. In the Public Analyst's general analysis he found the water to be normal and suitable for drinking and general domestic purposes, while in his particular analysis for chemical, physical or metallic irritants, phenolic substances, etc., he was satisfied that none was present. The bacteriologist was likewise satisfied that no organisms of the enteric or dysentery groups were present."

Plate 17

Walkerburn catchment area - the water intake is just beyond the cottage in the distance. The filter is on the right.

Plate 18.

Walkerburn - new filter in course of construction.

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In spite of the unpleasant appearance of the water "The Medical Officer of Health was satisfied that the outbreak was caused by a new type of virus infection". No virus studies of any sort had been carried out at this time. After this, special arrangements were made for virus culture for stool specimens.

Following this episode, the Public Health Authorities examined the Walkerburn filtration system in detail. It was found to be unsatisfactory. Details are given in a further extract from the 1959 Annual Report:

> "While intake, preliminary settlement and storage were found to be satisfactory, a heavy loss of water was detected in the slow sand filtration chamber which is in any case of inadequate capacity and incapable of maintenance. This necessitated the by-passing of this filter, water from the preliminary settling tank being discharged directly to the service storage tank. It is fortunate that the high class of 'raw' waters dealt with permitted of such an arrangement and the consumers were in no way endangered by the changeover as witness the bacteriologist's report on a sample taken subsequently.
>
> Number of viable bacteria per c.c. at 37°C. - 3
> Number of viable bacteria per c.c. at 22°C. - 71
> Presumptive B.coli (37°C.) absent from 100 c.c.
> Typical B.coli absent from 100 c.c. "

The County Council arranged to construct a new water filtration plant at a cost of £21,000 but because of financial restrictions this work was not begun until 1963. Water in the interval was supplied on by-pass as described. There was no chlorination plant, so for over four years this village was supplied by the County Council with unfiltered, unchlorinated water from a catchment on which sheep and cattle were grazing.

Apart from these County Council and Town Council water supplies, there are a large number of farms and country houses each with its own private water supply. These are usually from springs, but sometimes from surface water, collected into tanks of concrete, brick, or lead lined wood, and conveyed to the houses by pipes of iron, asbestos, copper, polythene or lead. Settlement and filtration in such systems may be unsatisfactory or almost completely lacking.

WATER ANALYSES

Limits proposed for lead content of drinking water.

1958 - World Health Organisation International Standard Limit:	0.1 p.p.m.
1960 - American Public Health Service Limit:	0.05 p.p.m.
1962 - American Water Works Association recommendation - an Ideal Water Supply should not exceed:	0.03 p.p.m.
1963 - World Health Organisation International Standard Limit:	0.05 p.p.m.

There is no direct legislation in Britain on this subject.

Water samples were examined for lead content for these studies by the Analyst to the Tweed River Purification Board using a standard Dithizone method. As an initial survey, water samples were obtained from three public and seven private supplies.

TABLE 1

Lead Content of ten different water supplies sampled within one practice on the same morning
(in parts per million)

Cottage	A.	0.46
Farm	B.	0.28
Railway House	C.	0.27
Private Estate	D.	0.125
Innerleithen Burgh	E.	0.05
Cottage	F.	0.04
Farm	G.	0.04
Farm	H.	< 0.04
Walkerburn-Priesthope	I.	Faint Trace
Walkerburn-Kirna	J.	Nil.

A considerable amount of water sampling has since been done from a total of 49 different houses and 25 different water supplies in the practice area, but an even greater number of small private water supplies to single houses remain unsampled. The samples were selected in an attempt to study the greatest concentration of lead in water to which patients might be exposed. Almost all were first morning samples (water which had been lying in the pipes overnight). Repeated samples were taken from houses with long lengths of lead pipe, with no mains tap (all water passing through a lead storage tank), and from supplies with very inadequate filtration systems. The table which follows relates the results obtained from all these analyses to the present and former International Standards. It can be seen that an excessive lead content has been recorded very frequently.

Three private supplies gave samples which exceeded 0.90 p.p.m. lead but the highest result of all, 2.7 p.p.m., was obtained from a house on Innerleithen Burgh water supply after plumbing repairs. Apart from this, the highest results from this water supply were 0.36 p.p.m. and 0.32 p.p.m. from two different houses, but from each of these, at some other time, lead analyses of morning water samples were reported as Nil. This great variability in range of results has made it impossible to estimate the lead intake of the population as a whole from water supplies.

Ingleson's (1938) method of extraction of the lead by a filter and subsequent estimation proved unsuccessful in practice, because the absorbent filter charge leaked through the filter which he recommended and part was lost. The great majority of the houses even if recently built are connected to the main by underground lead pipes even if the internal piping is of copper. The Public Health Authorities were kept fully informed of the water analysis results.

TABLE 2

Analysis of Water Samples for Lead

Total number of samples:	307
Lead content 0.05 p.p.m. or less:	134
Lead content over 0.05 p.p.m. and below 0.1 p.p.m.	53
Lead content 0.1 p.p.m. and more:	120

The range in pH in these water samples has been from 5.6 to 7.8.

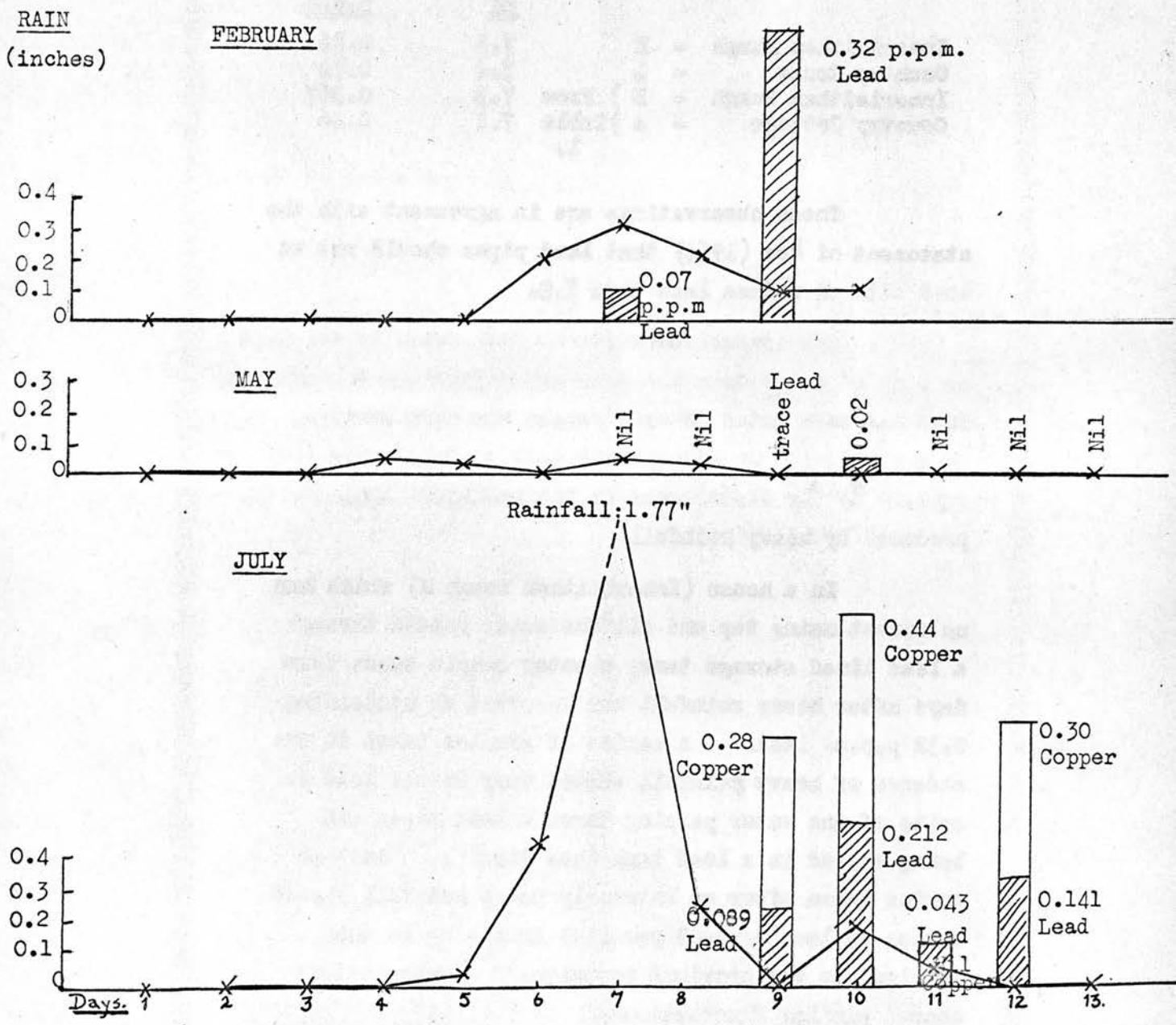
In addition to these the Water Analyst, for convenience in sampling, estimated for these studies the lead content of sixteen paired samples of water (before and after filtration), from Melrose Burgh water supply. This had a similar character to the waters in the practice area and presented similar problems.

Since two analysts had given different opinions on whether toxic metals were present, a third independent analysis was arranged at an early stage on four water samples and this confirmed the presence of abnormal amounts of lead (Hughes 1961). Various other laboratories which have helped in these studies have at times analysed single water samples. It can now be asserted that, though the bulk of the water analysis has been carried out at one laboratory, lead contents of more than 0.1 p.p.m. have been reported by six different laboratories from water samples from this practice.

The relationship between pH and plumbo-solvency.

From the pH estimations which were done along with all lead analyses it became obvious that pH 7 was not the division between the presence and absence of plumbo-solvent action. Sixty-six of the one hundred and seventy-three lead estimations above 0.05 p.p.m. were associated with a pH above 7.0.

Figure 5.



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In four cases the lead content was considerable.

TABLE 3

Alkaline Water Samples with High Lead Content

		pH	Lead as p.p.m.
Innerleithen Burgh	- K	7.5	0.26
Country House	- L	7.4	0.74
Innerleithen Burgh	- E) From	7.3	0.367
Country Cottage	- A) Table 1.	7.2	0.46

These observations are in agreement with the statement of Cox (1964) that lead pipes should not be used with pH values less than 7.8.

Considerable variations were found in the lead content of water from the same house from day to day. This has been noted by many people who have studied this problem. An attempt was made to relate the lead content to the disturbance in the catchment area produced by heavy rainfall.

In a house (Innerleithen Burgh M) which had no direct mains tap and all the water passed through a lead lined storage tank, a water sample taken four days after heavy rainfall was reported as containing 0.32 p.p.m. lead. A series of samples taken in the absence of heavy rainfall showed very little lead in spite of the water passing through lead pipes and being stored in a lead tank (see Fig.5). Another series taken after an extremely heavy rainfall showed a rise in lead content parallel in timing to that obtained on the previous occasion. Copper content showed similar fluctuations.

This shows clearly that in the month of May, Innerleithen water had virtually no plumbo-solvent tendencies but that heavy rainfall was associated with a considerable rise in lead content.

Water results in winter.

A long series of water samples taken in winter gave very different results from those shown in Fig. 5 for May. The samples were from a different house (E) but with a similar high maximum result (0.36 and 0.32 p.p.m.). Both houses were on Innerleithen Burgh water supply.

TABLE 4

Repeated morning samples from the same tap during two months in winter.

Lead content 0.05 p.p.m. or less	10
Lead content over 0.05 and below 0.1 p.p.m.	13
Lead content 0.1 p.p.m. or more	35
	58
Average	0.165 p.p.m.
pH range - 5.6 to 7.4. Average	6.8

In the above table and average one result of 2.7 p.p.m. has been included. This sample was obtained on the morning after a burst pipe had been sealed off by hammering. The burst was beyond the tap from which the sample was taken, but the vibration in the piping is presumed to have been responsible for this very high result.

These two houses (M and E) were detached villas with at least forty yards of underground lead supply pipe. The second was selected because of its similarity in age and appearance to the first.

House K (Table 3) on the other hand, was a first floor flat on Innerleithen High Street and it is likely that many of these will have similar lengths of lead piping. By estimating the appropriate time interval after rain, it was possible to obtain a water sample with a lead content of 0.26 p.p.m. This was the only sample taken from this house.

It may, therefore, be said that the water supplies of Innerleithen Burgh and the surrounding country area have a variable degree of aggressive action on lead supply pipes. This shows some relationship to the season of the year and to the rainfall. The lead content of the water, in consequence, frequently exceeds modern Internationally accepted standards of safety.

The influence of the time during which water lies in lead pipe on the lead content.

References have been made to the variability of this effect in the historical section(page[illegible]). A simple experiment was carried out to obtain some impression of the amount of this effect in Innerleithen Burgh water supply.

The water was run freely for five minutes from a tap on a lead piped mains water supply (House E) and a sample was taken. Two further 250 c.c. samples were then drawn off at long intervals without any other running of the tap between samples. A considerable increase in lead content occurred.

TABLE 5

Increase of lead content in water standing in lead pipe.

Date and Time of Sampling		Lead (as Pb)
30/9/62	5 p.m.	0.092 p.p.m.
	Midnight	0.258 p.p.m.
1/10/62	9.30 a.m.	0.367 p.p.m.

Further observations on Lead Compounds in Water Supplies.

Range of variation of Water Sample Results.

A number of water samples were taken from a farm which provided sample B, Table 1. In addition to a long length of lead piping this supply had a lead lined wooden tank on the hillside above the farm

for collecting and storing the water. One sample taken during the forenoon with no recent rain contained no lead. Samples taken before and after this showed very different results. They were taken either from the first running of the tap in the morning or at times when the water was brown and turbid. The highest result was from a particularly muddy afternoon specimen.

TABLE 6

Total number of samples	-	22
Maximum lead content	-	0.90 p.p.m.
Minimum lead content	-	Nil.
Average	-	0.198 p.p.m.
Number of samples above 0.1 p.p.m.	-	17
Number of samples between 0.05 and 0.1 p.p.m.	-	1
Number of samples below 0.05 p.p.m.	-	4

pH range 5.6 to 7.8.

Samples taken from the tank (Nil p.p.m.) and at the same time from the kitchen tap (0.256 p.p.m.) suggest that the length of the piping had a greater influence on the results than the lead lining of the collecting tap. Water was drawn from this tank by a lead pipe to the farm buildings and farmhouse and also by a copper pipe to three farm cottages.

Absorption of Lead by Sediment.

Reference has already been made to the occurrence, in water supplies in this area, of a brown sediment after heavy rainfall. When a sample of water containing sediment of this sort was submitted to a London analyst for confirmation of the presence of excessive amounts of lead, it was reported that the greater part of the lead was contained in the sediment.

TABLE 7

		Lead Content
a)	Clear water:	0.03 p.p.m.
b)	Calculated lead content of total sediment:	101 micrograms
c)	Calculated total lead content of original sample (470 ml.):	0.24 p.p.m.

Since 87 per cent. of the lead was in the sediment a very misleading result would have been obtained if this had not been analysed. This gives modern analytical confirmation for the comments of Alderson (1852) that lead could be absorbed in the sediment in water supplies.

The Sediment in the Walkerburn Water at the time of the 1959 Epidemic.

Samples of water and of the sediment deposited by a large volume of water on standing were taken at the time of the epidemic at Walkerburn in 1959. They were kept with a view to future study when some cause for this type of illness had been found. These were submitted for analysis by the Dithizone method in 1961 after plumbo-solvency had been suggested as a possible cause for gastro-enteritis.

TABLE 8

Analyses done in 1961 on samples taken in 1959 at time of epidemic

		Total Lead Content	Suspended Solids
Sample 1.	Water	0.23 p.p.m.	234 p.p.m.
Sample 2.	Water	Trace	123 p.p.m.
Sample 3.	Sediment only	>10 p.p.m.	

A visit was paid to the Public Analyst who had formerly done routine analyses for Innerleithen Burgh Surveyor and who had reported that organic matter was present, but no irritant metallic substances were found in the unpleasant looking Walkerburn water samples at the time of the 1959 epidemic of gastro-enteritis. On an enquiry as to the method of analysis used he said that he boiled down 500 cc. of water to 100 c.c. and then bubbled hydrogen sulphide through it. If there was a cloud then the metals specified (lead, copper and zinc) were present. If there was no cloud then they were absent. He subsequently said that the analyses were done on the water after filtering off the sediment and did not include the sediment. As I have just shown (Table 7) this could contain a large part of any lead present.

He stated that the method which he had described was in a book of methods approved by the Society for Analytical Chemistry. When the publication was consulted (Approved Methods for the Physical and Chemical Examination of Water, 1960), this was found to be incorrect. A different method was described - clearly headed "In the Presence of Organic Matter and Iron", which commences "Evaporate to dryness 500 ml. of water in a silica basin and gently ignite to remove organic matter present." Apart from the question of incorrect analysis, this method of removing organic matter must be borne in mind when considering observations which will be made later on the effects of prolonged boiling of water.

Stable Organic Lead Compounds in Water Supplies.

Mitchell (1963) observed that the probable presence of these may be inferred from the amount of lead passing through Ion Exchange Resin Filters and that fraction which passes through might be assumed to be in organic combination. He suggested that this might give some indication of the forms of lead in the water supplies which were being studied. Mitchell also commented that apart from fulvic and humic acids which are normal constituents of soil organic matter, there are probably many other organic materials which could form stable compounds with lead.

Using a commercial ion exchange filter recommended by its manufacturer for removing lead from water (containing cation exchange resin Zeo-Carb 225) the following results were obtained.

TABLE 9

Amount of lead passing through ion exchange resin filter
(Innerleithen Burgh Supply - E.)

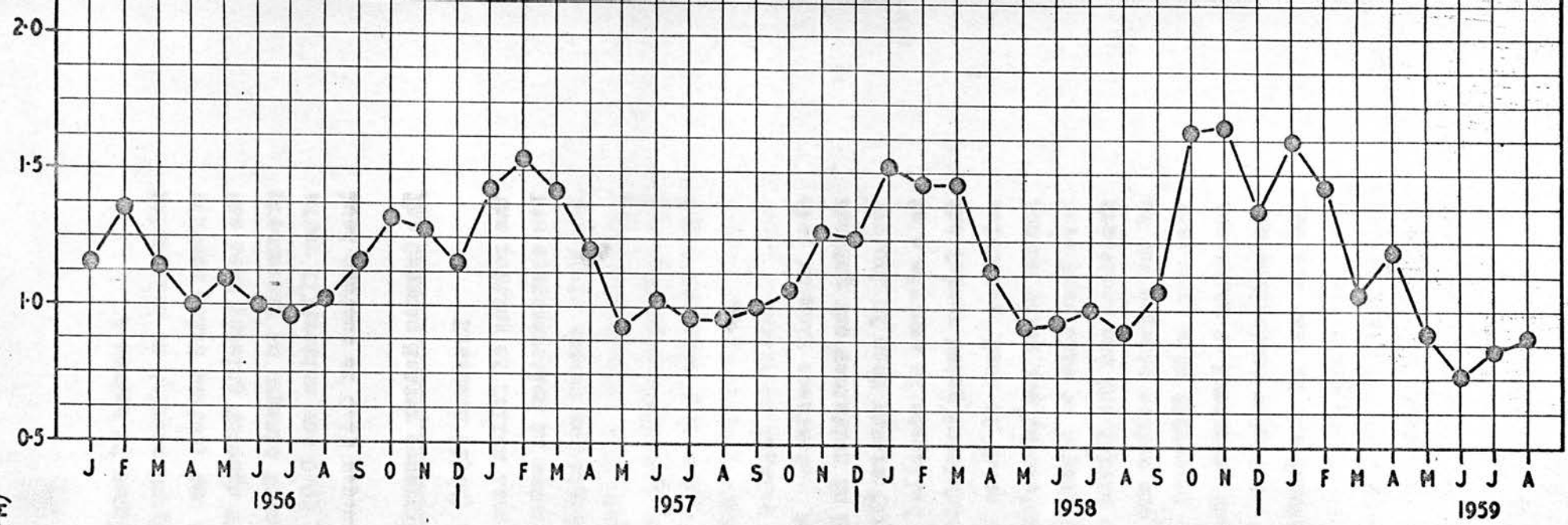
Unfiltered Water	0.289 p.p.m. lead
Slow filtration	0.06 do.
Fast filtration	0.07 do.

Other results using this type of filter showed that it extracts copper, but a small amount also passes through.

TABLE 10

Lead and Copper passing through ion exchange resin filter
(Supply - B)

	Cottage (copper pipes, lead collecting tank)		Farm (lead supply pipe, copper internal pipes)	
	Lead	Copper	Lead	Copper
Before filtration in p.p.m.	0.072	2.2	0.28	0.072
After filtration in p.p.m.	Nil	0.4	0.1	0.06



The vertical scale is a measure of the content of organic matter - the oxygen absorbed expressed in parts per million - a standard method for the estimation of organic matter in water.

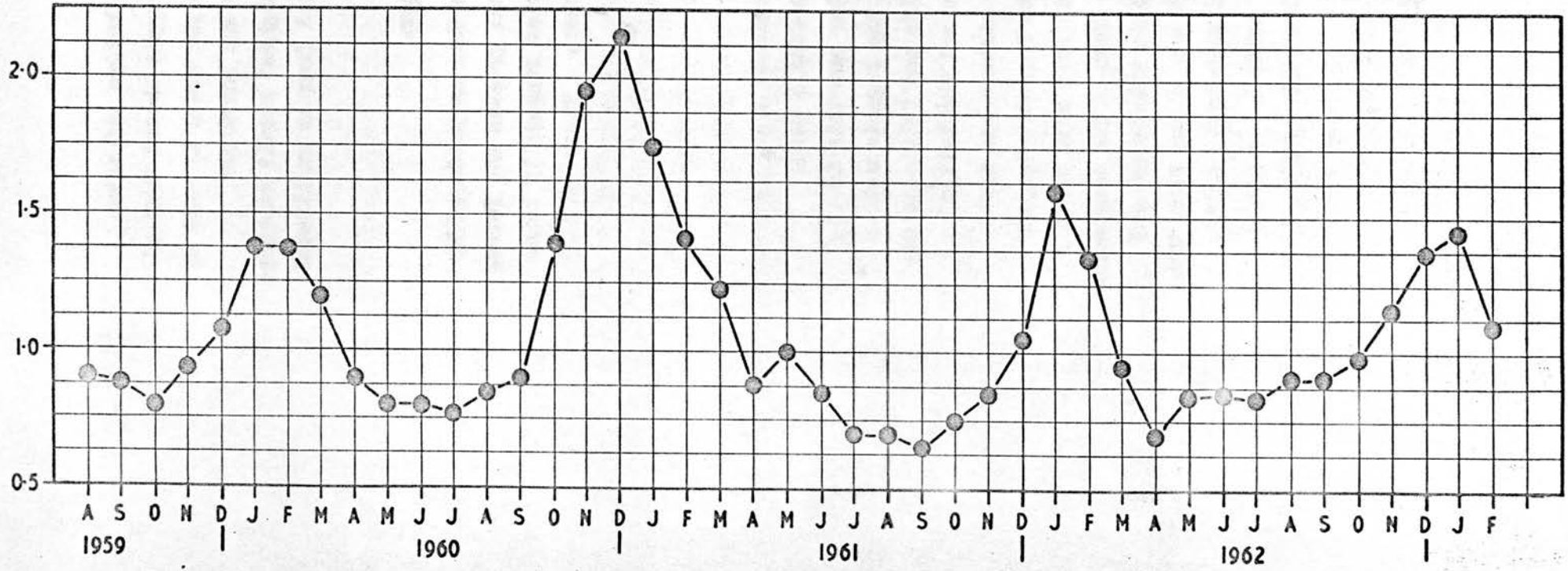


Fig.6 • Fluctuations in organic matter in water supplies. (OA-PPM)

A series of samples taken before and after filtration on Melrose Burgh water supply showed that of sixteen pairs tested, ten showed 20 per cent. or more of the lead passing through the filter and therefore presumably in organic form. The highest result recorded after filtration was 0.05 p.p.m. lead from an unfiltered lead content of 0.15 p.p.m.

The Organic Matter occurring in Water.

Kressman (1964) describes this as produced by the rotting of fallen leaves and dead grasses and ferns. Its concentration in water thus varies seasonally being lowest in summer and highest in winter. There is a rough correlation with the weather in the autumn when the rotting commences, a warm wet autumn giving a more rapid increase than a dry cool one. Since the vegetation is roughly constant from year to year the total quantity of organic matter produced every year is also roughly constant. He has provided a graph showing the variation in London water and this is typical of most waters (Fig. 6). The organic matter is a mixture of so-called humic acids and fulvic acids, the former being insoluble in acids and the latter soluble. Each of these is also a mixture and from London water the laboratories of the Permutit Company have been able to separate the humic acid into three fractions and the fulvic acid into four. The components of the organic matter are not specific substances and they vary with different waters but are of the same type. According to Kressman, they are all carboxylic acids, the equivalent weight of the humic acids being about 200 and that of the fulvic acids about 130 or 150. Humic acids are generally more darkly coloured than fulvic acids and fulvic acids contain a smaller proportion of carbon and hydrogen in their molecules than the humic acids and a greater proportion of oxygen.

Plate 19.

Copper salts of Humic and Fulvic acids (the fulvic acid salt is the lighter) with the original dried organic matter in the middle.

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Typical figures are:

	Humic Acids	Fulvic Acids
C	55%	50%
H	4.8	4
O	37	46

The organic matter forms quite stable salts and these can be readily converted from one to another. The Permutit laboratories were able to provide samples of the dried organic matter and of the copper salts of fulvic and humic acids (Plate 19). Similar salts were prepared with lead. In the opinion of Kressman, these are undoubtedly salts and there is no possibility of the metal being joined to any methyl or ethyl groups as it is in the lead tetra-ethyl which is used in petrol manufacture.

It was suggested by Sir Thomas Oliver in 1911 that lead compounds would be broken down in the stomach into the very soluble lead chloride.

As a result of discussions on this subject, Dr. Kressman agreed to attempt laboratory confirmation of this suggestion. Using the samples of lead salts of both fulvic and humic acids, he was able to confirm that they were readily soluble in cold dilute (0.IN)HCL from which were separated by warming, and then cooling, crystals of lead chloride. This gives some laboratory confirmation of what could be expected when the salts of weak acids are exposed to the action of hydrochloric acid in the stomach.

Other Observations on Innerleithen Water Supply.

On a number of occasions the Innerleithen Burgh water supply has contained minute gas bubbles in sufficient quantity to give the water a milky appearance when it runs from the tap. Though the water was so opaque that if a wash basin was filled the plug could not

be seen in the bottom, these bubbles very rapidly cleared.

On some occasions, patients have discovered water nymphs (Leuctra Hippopus) in the tap water and complained both to the doctor and to the Innerleithen Burgh Surveyor about this.

Routine chemical analyses done for the Burgh Surveyor were always reported as lead, copper, zinc and metals - none. Five years after it had been done, however, I was shown the report of a special analysis done for the Burgh Surveyor by the Permutit Company which had attracted no special attention at the time. The results included the following:

19 Dec.1958		
	pH	6.8
	Hardness Total	26 p.p.m. Ca CO_3
	Iron Total	Fe 4.4 p.p.m.
	Iron in Solution	Fe 0.05 p.p.m.
	Manganese	Mn 0.05 p.p.m.
	Zinc	Zn 0.06 p.p.m.
	Lead	Pb 0.05 p.p.m.
	Copper	Cu 0.05 p.p.m.

The iron content quoted is very high. Thresh, et.al. (1958) stated that "inconvenience" may arise from 0.3 p.p.m. of iron and when the amount exceeds 0.4 p.p.m. the installation of treatment plant is usually advisable.

Effects of boiling of water.

It is well known that if water is boiled till it is considerably reduced in volume, the qualitative detection of minute amounts of lead is made much easier.

It seemed possible that the domestic kettle, singing on the hob, might concentrate lead in a similar fashion. When this was tried experimentally with a kettle, however, the lead content fell from 0.25 p.p.m. before boiling to 0.06 p.p.m. after prolonged boiling. Some part of this was likely to be due to deposition on

the sides of the kettle. The experiment was repeated with a different sample under laboratory conditions and the analyst reported that part of the lead in the sample had volatilised.

TABLE 11

Loss of Lead on Boiling Water

Volume	Lead (p.p.m.)
150 mls.	2.7 (Sample from House 'E').
75 mls.	2.39
27 mls.	1.37

Another laboratory has since provided confirmation of this unexpected finding of a volatile lead compound in water supplies by distillation and has also done a detailed analysis on the sediment from Innerleithen water.

TABLE 12

Distillation of Lead from Water Samples

	Untreated Sample (p.p.m. Pb)	Distillate (p.p.m. Pb)	Residue (p.p.m. Pb)
Sunbury tap water (control)	0.072	0.024	0.059
Innerleithen water			
11.30a.m. 4/8/62	0.03	Nil	0.037
1.30p.m. 4/8/62	0.03	-	-
11.30p.m. 4/8/62	0.10	0.051	0.097
8.30a.m. 5/8/62	0.06	-	-

It will be noted that while an appreciable amount of lead was distilled across with one sample from Innerleithen, none was obtained from the other. An Edinburgh Biochemical Laboratory (Lab. N.*) has also attempted distillation of a heavily sedimented water sample from this practice. This contained 0.13 p.p.m.

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* Lab. N. - Laboratory of the Northern General Hospital, Edinburgh.

lead but there was no evidence of any volatile lead compound on distillation. It is also worthy of note that not only was lead distilled from the control sample of Sunbury-on-Thames tap water but the untreated sample exceeded the present World Health Organisation limit for lead content.

Analysis of Distillate and Residue from Sediment from Innerleithen Water Supply.

To avoid the necessity of sending a large volume of water from Peeblesshire to Sunbury-on-Thames for extraction of the sediment, this material was obtained from the bottom of a glazed toilet cistern at the end of a lead pipe-line. (Some glazes are known to contain lead.) There was a considerable quantity of brown sediment accumulated over three years since the cistern was installed, and a large sample was easily obtained.

For this analysis the sample was distilled into two fractions. The first fraction to be examined by Infra-red methods, was the distillate which would contain any volatile lead compounds. The residue was extracted with water twice and with carbon tetrachloride. These were examined. The insoluble residue remaining after water and carbon-tetrachloride extraction was examined by separation into fractions depending on the density.

Each of the fractions was analysed by Infra-red spectroscopy and some of them were analysed by X-ray diffraction and fluorescence techniques, and the results were tabulated.

TABLE 13

Sediment from Innerleithen Water Supply

Fraction	Infra-red	X-ray Diffraction	X-ray Fluoresence
1. CCl_4 extract of distillate	Only a small quantity of organic material present	X	X
2. First H_2O extract of residue	Sulphate and possibly carbonate	NaCl gypsum and soluble $CaSO_4$ present	Major Br Mc Ca
3. Second H_2O extract of residue	Present in both extracts		Minor Sr Cu I Zn Pb Fe Cl K
4. CCl_4 extract of residue	Contains a very small trace of organic material	X	X
5. CCl_4 and H_2O insoluble residue density fractions	The IR spectra of these fractions were very similar. They all contain quartz and probably inorganic sulphates	All fractions gave similar results: - The main components are: quartz (SiO_2) illite and probably a type of chlorite.	
A			A Major Pb Fe Br
			A Minor Zn Cu Sr K Ca
B			B same as A
C			"
D			"
E			E Major Fe
			E Minor Pb Br Zn
F			F Major Fe Pb Br Cu Zn
			F. Minor Sr Mn Ca K Ti

It can be seen that from the sample of sediment obtained in this way, only a small quantity of organic material was extracted. A considerable range of heavy metals was identified. One of the main components of the insoluble residue was quartz (SiO_2). The inhalation of Silicon Dioxide (Silica, SiO_2) and its absorption from the lungs are known to produce Pulmonary Fibrosis. Coope (1946) described silica in solution as a protoplasmic poison in the lungs giving rise to necrosis or fibrous reaction. On the other hand, silicates (such as Magnesium Trisilicate) are frequently used in treatment for Peptic Ulceration, and Thresh, et.al. (1958) are of the opinion that the presence of silica in water has not been shown to have any effect whatever on its purity and wholesomeness.

Other water supplies referred to in these studies.

For purposes of comparison, it became necessary to extend studies of non-industrial urine coproporphyrin excretion beyond the practice. Enquiries were made about the water supplies of three areas as part of the planning of these extended studies.

Edinburgh City Water Supply: A visit was made to the Edinburgh City Analyst who said that corrosive effects of Edinburgh water on metals had only been brought to his notice in two connections. He agreed that the water had some corrosive properties as shown by iron staining of water running from iron W.C. cisterns. The least trace of iron in water precipitated tannin in whisky and he had had complaints from firms dealing with whisky about this. He had also a complaint about the zinc content of Edinburgh water from a laboratory worker in the University Department of Zoology who was not being successful in growing snails which are extremely sensitive to zinc.

He was asked for analysis of the zinc content of the water but this proved to be too small in amount for the sensitivity of the methods used by the City Analyst. The analyst was quite satisfied that householders should run their taps in the morning to displace the water which had been lying in the pipes and was most emphatic that if anyone cleaned out and scrubbed out a lead lined storage cistern in Edinburgh and then used it for drinking water they would get lead poisoning. On this point he was very definite. He used a simple sulphide test - passing H_2S through the water - without any boiling to concentrate metals. He regarded this as a very sensitive test. He did not consider important any amount which failed to show up on this test.

The City Water Engineers Department provided a lengthy table showing the results of the monthly chemical analyses for the year, October 1960 to September 1961. The results were expressed in parts per 100,000. The columns for iron, and for lead or other poisonous metals, were occupied only by hyphen marks (instead of nil or none detected). Minimum pH values from 6.5 to 6.8 are noted in seven of the ten places from which samples were taken. The water supplies from Torduff and Clubbiedean are considerably harder and more alkaline than the very soft water supplied from Talla and Gladhouse Reservoirs. The Currie area is supplied with these harder, more alkaline waters from the North Pentland Springs and as far as the Corporation Water Engineers are concerned there has never been any suggestion of plumbo-solvency with these supplies. This information was used in arranging a control series of samples from maternity patients.

<u>Inverurie, Aberdeenshire</u>: The water supply to this town was described by the Burgh Surveyor to one of the doctors practising in the area, as coming from

four sources with an average pH of about 6.5. The sources vary from deep springs to water from a mountain burn. My information, dated 1/8/63, (Gill 1963), stated that in 1961 when the last analyses were performed no poisonous metals were found. All supply pipes from the main were of lead. Apparently the Burgh Surveyor in this town insists upon this.

Melrose: In 1961/1962 a number of water samples from the Burgh of Melrose were reported as chemically doubtful or chemically unsatisfactory because they were plumbo-solvent or potentially plumbo-solvent, being soft and acid. Minimum figures of pH 6 were recorded and one sample had a lead content of 0.74 p.p.m.

Discussion.

Certain defects in the water treatment processes for Innerleithen and Walkerburn have been mentioned. The County Council, faced with complaints about water quality at Walkerburn, obtained the advice of consultant engineers and adopted a modern water treatment installation with chlorination, costing £21,000. This is for a community of approximately 1,000 persons, but the County Council draw Rates from a very much greater population (14,156). In contrast Innerleithen Burgh Council made alterations and improvements to the existing filtration system at the cost of £1,000. A more appropriate solution to the water supply problems of the area would appear to have been a regional scheme to supply both town and village which are only two miles apart.

The Innerleithen Burgh supply, even after improvement was a process of gravity filtration through gravel. There is no question of this being either slow sand filtration or rapid sand filtration because the minimum size of the gravel described by

the Burgh Surveyor far exceeds even the 0.8 mm. sand which Thresh, et.al. (1958) suggest for filters used as coarse strainers preparatory to slow sand filtration. The depth of a sand bed should usually be 2½ to 3 feet on a supporting layer of gravel and the depth of water on top of the sand 5 to 6 feet. Therefore, even after the improvements the charge could be levelled at the Innerleithen water treatment process that it acted merely as a coarse strainer and not as a true filter in ths usual sense of the word. Deterioration in the character of the water of the type illustrated in Plate 2 can only be described as extremely unsatisfactory especially in view of the absence of chlorination.

Standards of safety for the lead content of water are being progressively lowered because of the improvements in the technique of water treatment, and in the light of modern knowledge on the effects of lead. Davidson (1933) found it very difficult to get a clear opinion on a safe level for lead content of water, and Ingleson (1934) quoted opinions ranging from 0.1 p.p.m. having caused poisoning to 1 p.p.m. after twelve hours contact being safe.

The Water (Scotland) Act (1946) lays upon every local authority the duty of providing a supply of wholesome water to every part of their district where a supply of water is required for domestic purposes, but adds the most important phrase "and can be provided at a reasonable cost". This should ensure a satisfactory supply to towns and villages, but isolated farms and shepherd's cottages are unlikely to qualify, though help may be provided for these by improvement grants from the Department of Agriculture. Many of the innumerable small private supplies were laid down prior to the beginning of this century. If the water is very aggressive, the piping may burst so frequently that it has to be replaced and this is likely to be done with more modern materials than lead.

The main concern of the countryman is that his water supply shall be available all the year round and shall not run short at times of drought. He expects to keep to a minimum, the cost of piping and does not wish the expense of drilling or installing a pump. If his water supply is occasionally discoloured, he is not disturbed because of the widespread belief that no harm can come from water which has been boiled.

To circumvent the discolouration of the water supply, many country people use their hot water systems at times of heavy rainfall, thereby interposing two additional tanks to act as settlement chambers between themselves and their source of supply. The cold water storage tank may be lead lined and the hot water pipes may also be of lead. The increased risk of filling kettles from a lead piped hot water system has already been mentioned.

One of the countryman's criteria for judgment is the taste of the water, but a water which he favoured would not necessarily be one which an analyst would consider ideal. For example, one farmer in this practice lamented that the water in his present farm did not taste as good as that in a farm he had had previously. When asked about the previous farm it was discovered that it was farm B on which extensive water sampling had been carried out, with a maximum lead content of 0.9 p.p.m. If there is an aggressive water and iron piping in the system, there may be complaints of the taste of the tea, because of the precipitation of tannin in the tea. Only if an improvement grant is sought is the water tested in any way. This is likely to be done by a Public Health Inspector in the course of his daily visits. The routine of first flaming the tap, then running it for five minutes, and then taking a bacteriological sample has been well taught, and the sample for

chemical analysis will be taken either before or after this ritual. If it is taken after, then the chances of detecting lead are very much reduced.

While an increase of the lead content of water on standing in lead pipes is not a constant feature the experiment in Table 5 was done to make some assessment of the amount of such increase, which was likely in this practice. It has already been noted that rapid transit of water through the pipes is not necessarily a protective measure. Thresh, et.al. (1958) commented that water samples, after long standing in lead pipes, may contain less than after a short period due to particulate lead compounds not being flushed into the sampling bottle. All that can be said from this experiment is that on this occasion the lead content trebled in seven hours and quadrupled in amount in sixteen hours.

From the lead analyses to two houses on Innerleithen Burgh Supply it can be concluded that plumbo-solvency is minimal in that supply in summer except after heavy rain, but is much more constant in winter. The extreme range of winter pH down to 5.6 is notable, and in contrast to the results obtained after the addition of lime.

The effect of interference or repairs on the piping is very clearly shown by one analysis, reporting a lead content of 2.7 p.p.m. This gives a good illustration of how gross contamination could occur which would not be identifiable by subsequent analyses.

Absorption of lead by the sediment in water was known in Alderson's time over a hundred years ago, but we have been able to provide laboratory evidence of the amount of this. It has not been sufficiently noted. It assumes great importance in these studies partly because the original analyst, apparently, being aware that organic matter interfered with his hydrogen

sulphide test, overcame this difficulty by filtering it off and testing only the filtered liquid.

From Table 8, it can now be said that there was in Walkerburn water at the time of an epidemic of gastro-enteritis a considerable amount of sediment of organic nature. This is known to absorb metals and a sample of such sediment contained a large quantity of lead. No estimation was made of the copper content of the sample. In fairness to the original analyst, it should be observed that Thresh et.al. (1958) stated that so far as is known there is no reliable evidence that organic matter in treated water is harmful, in the absence of specific pathogenic bacteria and other specific toxic agents. No such toxic agents were found, but the methods used now seem to leave much to be desired.

Volatile lead compounds in water.

Since some methods of lead analyses from organic materials make use of a muffle furnace at 450°C. it was most surprising to get a loss of lead at 100°C. Mere loss of lead on boiling is not sufficient proof of volatilisation, but this is provided by the distillation experiment. A volatile lead compound (or compounds) was present in one Innerleithen sample but not the other and also in a sample of water from Sunbury-on-Thames used as a control. It is interesting to note that the Sunbury water sample exceeds the current World Health Organisation International standard for lead content in drinking water. The detailed analysis from the Sunbury laboratory is of interest, but gives no definite evidence of a single specific gastro-intestinal irritant.

From the experiments with ion exchange resin filters, and the experiment of Kressman, we may conclude that up to one third of the lead may be as salts of humic or fulvic acid and likely to be converted

into highly soluble lead chloride in the stomach. Bell, Davidson and Scarborough (1959) described the absorption of iron in food as first, conversion to soluble, diffusible ferric chloride, and then reduction to ferrous chloride prior to its absorption. Iron in organic combination is utilised to a limited extent only. Information on local irritant effects in the gut and on relative toxicity of lead chloride compared with other lead salts is lacking, but the chlorides of zinc, barium and mercury are highly irritant.

Lead, however, is not the only metal occurring in these water supplies though it is the most toxic. It seems possible that the combined astringent effect of iron, zinc, manganese, lead and copper in varying proportions might cause the gastro-enteritis which stimulated these studies in the beginning. It is difficult to obtain information about the minimum quantities of these metals which would be expected to cause gastro-intestinal symptoms.

An abnormal incidence of vomiting in school-children, plus the death of fish in tanks, caused some investigations to be made in 1957 in a school on Edinburgh water supply. A copper content of 7.9 p.p.m. was recorded with a pH of 6.0. The following factors were believed to contribute to this episode. (Laurenson 1963)

1. The new copper piping in the school.
2. The defective functioning of a pH gauge at the water works which resulted in inadequate correction of the pH which was normally maintained about 7.
3. The earthing of D.C. Laboratory equipment to the water mains.

It is difficult to asses how widespread is the problem presented by plumbo-solvency. It has been shown to have been definite in Melrose, and a sample from Sunbury-on-Thames exceeded the present International standard limit. Brown (1946) gave evidence of considerable exposure to lead from Glasgow water supplies reaching hazardous levels in some parts of that

city. From the Department of the Government Chemist, Johnston (1964) suggested that the Loch Katrine supply to Glasgow is distinctly plumbo-solvent and it was likely that distribution points on long lengths of lead piping would provide higher lead results than those found at Innerleithen. Edinburgh and Inverurie are both open to criticism from the pH aspect, though no lead estimations are available.

A great deal depends on the water sampling methods and on the analytical techniques used. If we accept Ingleson's comment that all lead piped water contains lead, then it is a matter of analytical sensitivity. As an example of the minute quantities of metals which can be estimated in water, it was noted that Mitchell (1963) gave the copper content of Aberdeen water after distillation as 0.0003 p.p.m. With an International Standard for lead of 0.05 p.p.m. there can be little place for a method of analysis whose minimum sensitivity is 0.1 p.p.m. If analysts adopted more sensitive methods and gave more exact figures for lead content, however slight, then lay water committees might well become apprehensive when presented with reports showing the presence of lead in their water supplies.

Wood suggested that the implementation of the former 0.1 p.p.m. International Standard could cause great difficulties in Britain, and Hoather stated that there had been in the past widespread inadequate treatment. There is no reason to doubt either statement.

The most recent reduction in the International Standard for the permissible limit for lead content has produced a situation in Britain where we can no longer say that plumbo-solvency is of largely historic interest. The difficulty lies in the proof of resulting harm at such low levels of exposure.

The Lead Content of Milk.

One simple method for the treatment of mild cases of lead poisoning is an increase in the daily consumption of milk. Hunter (1957) suggests that two pints per day (or a daily dose of 10 gm. of calcium lactate) is all that is necessary to store lead in the bones so that it will not be free in the circulation. For cases with "toxic symptoms" he recommends four pints of milk daily plus 15 gm. Calcium lactate, whereas "in the presence of acute symptoms" the patient should be treated in hospital by intravenous calcium ethylene diamine tetra acetate.

Where the water supplies contain an abnormal amount of lead, the substitution of milk for water could be expected to have the additional advantage of reducing the total lead intake. However, in winter, milking cows are kept in byres and may be supplied entirely with lead-piped water. In summer they are likely to drink also from rivers and streams. The normal daily water demand of a cow in milk is thirty gallons per day (Wilkinson and Squire 1960). It, therefore, seemed necessary to discover the effect on the milk of a water supply such as that of Farm B, where the lead content could rise to 0.9 p.p.m. Allcroft, R. (1950) states that cattle have tolerance to relatively enormous quantities of lead.

A sample of milk from a cow on Farm B. was reported as having a lead content of 0.94 p.p.m. (Cow 1.) Immediately after this was obtained the cow became unwell and the milk stopped for a few days. This illness was described by the farmer's wife when arrangements were being made for a further series of six samples. These were obtained from three cows (including Cow 1) direct from the teat, from Cow 1 milked into a galvanised bucket, passed through a cooler and stored in an earthenware kitchen jug, and from the milk sold by two Innerleithen retailers. The samples were sent to the Royal (Dick) School of Veterinary Studies at a time when the Toxicology

section was in the course of removal to a new building. It was subsequently discovered, as already mentioned, that a series of copper analyses being done at this time and also involving a Dithizone extraction were giving false results.

TABLE 14.

Milk Samples - Series 1

The report on these six samples was:

Cow 1. - 0.42 p.p.m.	Cow 1. from jug - 1.52 p.p.m.
Cow 2. - 0.45 p.p.m.	Retailer A. - 1.30 p.p.m.
Cow 3. - 0.47 p.p.m.	Retailer D. - 1.46 p.p.m.

"We have made a small survey of milk from our own farm after it has been milked into a bucket and sampled from there. The mean value is 1.36 p.p.m. lead and the Standard Deviation ± 0.19." (Barden 1961).

This laboratory staff have ample experience of lead estimation, since lead is still the most common cause of poisoning of livestock in Britain. (Lecture notes for students - Royal (Dick) Veterinary College, 1962). They receive a steady flow of blood and tissue samples from between 30 and 50 animals suspected of lead poisoning each year. They had been unable to trace any figures for the normal lead content of milk in the veterinary literature. This was the reason for the control series from their own farm.

These results were disconcertingly high and after some enquiries, further samples were sent in duplicate to the same Edinburgh laboratory and the Central Veterinary Laboratory of the Ministry of Agriculture at Weybridge, Surrey. Dr. Allcroft of the latter laboratory reported that all the values in the second series were low and in what she regarded as the normal range.

TABLE 15

Milk Samples - Series 2.

		Edinburgh	Weybridge
Cow 1. (B Farm)	From	0.120 p.p.m.	< 0.05 p.p.m.
Cow 3. do.	teat	0.09 "	< 0.05 "
Cow 4. do.	direct	0.009 "	0.06 "
Cow 4. Milk prepared and in jug ready for use.		0.135 "	0.09 "
Retailer A.	Milk from bottle	0.09 "	< 0.05 "
Retailer B. 1	as retailed in	0.045 "	< 0.05 "
B. 2	Innerleithen	0.09 "	< 0.05 "
Retailer D		0.045 "	0.06 "
Retailer D. 1	The two farm	0.09 "	0.06 "
D. 2	supplies of retailer D.	0.225 "	0.06 "

A further five samples were sent to Weybridge along with an enquiry on whether more exact figures below 0.05 p.p.m. could be provided. The reply was that in order to obtain any meaningful figures to the third decimal place, very much larger volumes of milk would have to be used than their usual 5 ml. quantities. This would lengthen the time for each estimation very considerably and neither time nor staff were available for this. Figures in the third decimal place, or even in the second decimal place would have little or no value at amounts below 0.05 p.p.m. by the method used. The observation of McKellar (1964), see p. 53 , on blood lead results from this laboratory would seem in agreement with this comment. The Edinburgh laboratory used 100 ml. milk samples for each analysis.

TABLE 16

Milk Samples - Series 3

		Edinburgh	Weybridge
A.		0.06 p.p.m.	<0.05 p.p.m.
B.	All four Innerleithen	0.038 "	<0.05 "
C.	retail milk supplies.	0.08 "	<0.05 "
D.		0.054 "	<0.05 "
E. - Private estate supply.		0.09 "	<0.05 "

Discussion.

The first milk sample from the ailing Cow 1 may or may not have been correct. If it was, then with this lead level the cow was suffering from lead poisoning. This would not be at all unlikely judging from the normal water demand and the lead levels found in this water supply. From the subsequent observations, the results in Series 1 are obviously faulty and seem likely to have been caused by contamination in the laboratory resulting from the disruption of the removal to new premises.

Series 2 and Series 3 present the problem of conflicting results from two competent laboratories. The one was using a method which was taxed beyond its lower limit (0.05 p.p.m.) by the samples supplied and the other had previously provided results whose accuracy was suspect. It is necessary to recall the observations of Kehoe (1961) on the difficulties of dividing urine samples (see page 52). Milk with its cream content is not a homogeneous material and this could account for the variation in the results. It seems reasonable to infer that the range of lead content in the milk supplies in the practice is from 0.038 to 0.09 p.p.m. A milk sample analysed along with food samples in yet another laboratory contained 0.05 p.p.m. lead.

References to the normal lead content of milk in the literature are very scanty. Kehoe (1961, [redacted]) reports three samples with a range 0.02 to 0.04 p.p.m. Schroeder et.al. (1961) found no lead in "fresh local whole milk". White, Clifford and Calvery (1943) give the milk from three normal cows as containing 0.030, 0.028 and 0.030 p.p.m., and Blaxter (1950) reports the milk from one cow as having a lead content of 0.02 p.p.m.

One sample of human breast milk was obtained. It was expressed into two sterile universal containers. These were reported by the laboratory concerned (Lab. G.)* as containing

1. 4.19 µg/100 G. (0.04 p.p.m.)
2. 2.46 µg/100 G. (0.02 p.p.m.)

The patient who supplied this sample had a blood lead level of 46.69 µg/100 gm. (laboratory normal - 22.9 ± 8.2 µg/100 gm.) and urine lead 72.5 µg/litre (laboratory normal 23.3 ± 12.5 µg/litre). The urine coproporphyrin reading was 3½ degrees on the Donath Scale (100-200 µg/litre). Further comment on this patient will be made later.

The significance of the lead content of milk will be discussed along with the food analyses.

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* Lab. G. - The Laboratory of the Gardiner Institute, Western Infirmary, Glasgow.

Lead in Soil and Vegetables.

Lead has been mined in the past in the Southern Uplands of Scotland. The Leadhills, described by Wilson in 1754, lie fifty miles to the southwest of Innerleithen and Leadburn is fifteen miles northwest. With this in mind, the Medical Officer of Health arranged lead analyses for water samples from the intakes of Innerleithen and Walkerburn water supplies, but no lead was detected.

At a later date it was discovered that a very small old leadmine lay within the practice area. This was marked on the larger scale Ordinance Survey maps on the hillside above one branch of the Fingland Burn. The remains of the mine consisted only of a small hollow and a pile of loose stones about ten feet

high. It did not suggest very extensive workings. A water sample taken from the adjacent branch of the Fingland Burn contained Lead 0.024 p.p.m. If the Fingland scheme had been adopted by the Burgh of Innerleithen, this would have been an additional source of lead intake for the population.

It seemed prudent to discover whether the soils in the practice area had a high lead content. Home grown vegetables in such an eventuality might add appreciably to the total lead intake of the patients. A small series of soil samples was taken from gardens in widely separated parts of the practice from the water catchment areas, and from the old leadmine itself. Estimation of the acetic acid extractable lead was done by Spectrographic methods at Edinburgh University School of Agriculture.

The Analyst's assessment: "The lead status is based on results obtained with a large number of agricultural field soil samples from South East Scotland. For such samples the acetic acid extractable lead content does not normally exceed 3.0 p.p.m. and the level is over 2.0 p.p.m. in only about 5 per cent. of the number examined.

In the following table, most of the high lead values are associated with garden sources and it may be that garden soils, in general, tend to have higher lead contents as a result of contamination".

TABLE 17

Soil Results (26th July 1963)

	Acetic Acid extractable (lead (p.p.m.)	Status
Garden A.	8.69	Very high.
Garden B.	0.69	Normal.
Garden C.	3.72	Very high.
Garden D.	3.43	Very high.
Garden E.	0.27	Normal.
Garden F.	0.40	Normal.
Catchment Innerleithen - main	0.70	Normal
Catchment Innerleithen - subsidiary	1.54	Rather high.
Catchment Walkerburn-Priesthope	2.44	High.
Old Leadmine	1.47	Rather high.

Of the three gardens from which very high results were obtained, one ('C') was not well tended. Vegetables were rarely grown and it was situated over a former refuse tip. The other two such results 'A' and 'D' were from the well tended, well manured vegetable plots of keen gardeners. In garden 'A' there were possibilities of contamination from petrol fumes and from a garden hose on the end of a very long lead pipeline.

Two cabbages were obtained from the plot in garden 'A' which had shown the highest results. They were analysed at the same time as two cabbages purchased in Edinburgh. The Innerleithen cabbages were found to contain considerably less lead than the Edinburgh ones:

Innerleithen cabbages: 0.22 p.p.m. and 0.21 p.p.m.
Edinburgh cabbages: 0.38 p.p.m. and 0.27 p.p.m.

The subject was, therefore, pursued no further.

Lead in Food.

It was appreciated from an early stage in these studies that the lead absorbed from the water supplies formed a part only of an indefinite total lead intake. When all the other studies had been completed facilities became available for estimation of the lead content of foodstuffs. The Occupational Hygiene Service of Manchester University Nuffield Department of Occupational Health undertook the analysis of a complete two-day diet. This laboratory has a great deal of experience with lead analyses handling over 1,500 each year. The diet was prepared by a trained dietitian in Innerleithen whose domestic water supply has already been described. This supply (M.) all passed through a lead lined storage tank and so was likely to be less subject to fluctuations in lead throughout the day than most others. The maximum result obtained from this house on previous sampling was 0.32 p.p.m. (Fig.5). The illnesses of this family and their dog will be described later,(page 27).

The samples sent originally were in correct quantities. All the tinned foods had been emptied from their original containers. The analyst found that soup, baked beans and ravioli all gave results exceeding the legal limits for lead in food, and asked for repeat samples in unopened tins. Multiple analyses were done on these and very different results obtained. The analyst now suspects that with a gross excess of tin, the method used for the first specimens could give an excessive estimation of lead (King 1964).

TABLE 18

	2 day amount (Gms).	Lead as Mg/Kg	Lead content of 2-day diet (Mg)	Repeat estimation Mg/Kg	Revised Lead Content (Mg)
Milk	1136	0.05	0.057		
Soup	426	5.5	2.339	0.3	0.128
Baked Beans	227	9.0	2.043	0.56	0.127
Ravioli	191	4.1	0.783	0.62	0.118
Baked Potato	170	0.74	0.126		
Cabbage	142	0.12	0.017		
Pear	113	0.1	0.011		
Apple	142	0.1	0.014		
Tomato	85	0.03	0.003		
Jelly	296	0.35	0.104		
Egg	57	0.24	0.014		
Sausage	128	0.38	0.049		
White Bread	198	0.76	0.150		
Brown Bread	64	0.26	0.017		
Beef	85	1.7	0.145		
Boiled Potato	142	0.32	0.045		
Gervais Cheese	57	0.10	0.006		
Cottage Cheese	57	0.40	0.023		
Tea	14	0.79	0.011		
Coffee	21	2.1	0.044		
Water	3469	0.13	0.443		

Total for 2 days - 6.444
Revised Total for 2 days - 1.652.

Daily intake - 3.222
Revised Daily intake - 0.827.

Attention having been drawn by the first results to the possibility of tinned foods containing excessive amounts of lead, three foods used for babies were sent along with the other unopened tins.

The results - by the revised analytical method were:

Condensed Milk	- 0.84 p.p.m.
Baby Tomato Soup	- 0.7 p.p.m.
Baby Bone and Vegetable Broth	- 1.2 p.p.m.

From the manufacturer's directions, an estimate may be made of the lead intake of babies up to the age of three months on evaporated milk, bone and vegetable broth (at the stage when this is added to the diet) and water. The level of the World Health Organisation Standard Limit (0.05 p.p.m.) has been used as a basis for water calculations. Sugar has not been included because there are no figures available from these food analyses. (The other foodstuffs analysed had been sweetened and prepared ready for eating, so sugar does not appear as a separate item). For purposes of comparison an estimate has been made of the lead intake for a 70 Kg. adult, which would correspond to these baby lead intakes on a Mg. per Kg. basis.

TABLE 19

Calculated Lead intake of babies under three months

Baby Weight	Lead Content of Condensed Milk (Mg per day).	Lead from Water at 0.05 ppm (Mg per day).	Bone and Vegetable Broth Lead Content (Mg per day)	Total lead intake per day	Approx. Equivalent for a 70 Kg Adult
6 lb.	0.14	0.021	-	0.16	) 4 Mg per day
9 lb.	0.21	0.026	-	0.23	)
12½ lb.	0.29	0.032	0.038	0.36	)

Lead in Milk and Food - Discussion.

Monier Williams (1938) calculated that the maximum permissible limit for the total daily intake of lead should be 0.75 to 0.80 mgms. Kehoe (1961) stated that the quantities of lead in the food and beverages available to the population should be such that individuals may choose what they will in quality and quantity, without running the risk of ingesting more than 0.6 mgms. of lead per day on the average over any prolonged period of time (years).

Kehoe's studies are the most complete on this subject and he estimated the normal daily intake of lead in food for the North American as about 0.3 mgms. He calculated that it would take between seven and nine years consuming an additional 1 mgm. of lead per day to raise the blood lead content to the level at which he considers poisoning occurs (80 µg/100 ml.) He does, however, indicate that the onset of intoxication often coincides with the occurrence of a sharp increase in the rate of absorption of lead by the individual, and suspects that the trigger mechanism of lead intoxication is the overburdening of the tissues with unbound or ionic lead either through an unduly rapid rate of absorption or by mobilisation of lead previously stored in the tissues.

If we wish to search for the first signs of physiological variation from normality arising from lead then we must accept Kehoe's lower figure of 0.06 mgms. as a limit of safety, for this is the level at which he records the building up of stores of lead as just being recognisable. Some confirmation of these observations is provided by the experiments of de Langen and ten Berg (1948). Giving groups of human volunteers two-thirds of a mgm. of lead in water first thing each morning, they found the urine contained a clearly increased amount of coproporphyrin after about three and a half

months. The addition of only one-third of a mgm. per day to the diet gave no rise in urine coproporphyrin after seven months. These authors also noted that if the lead was given along with food, the reaction took twice as long to develop as when given on an empty stomach first thing in the morning.

These known amounts of lead were added to the unknown lead content of the food and drink of the Dutch volunteers and the results represent the effect of the total amount absorbed from all sources. A considerable difference was found between the lead content of the specimen diet from Innerleithen and the average figures given for the United States. It might be unwise therefore to presume that Dutch and American diets had the same lead content.

The Innerleithen diet certainly gave figures well above Kehoe's level of safety. Continued consumption of lead at this level might be expected in the long run to cause trouble. The lead intake from a number of the items in this diet could vary but the biggest variation is likely to be related to the water.

Deterioration of water quality at the house from which the diet was obtained could provide a lead intake from water alone of 0.54 mgms. per day. It certainly seems possible that this could provide the "sharp increase in the rate of absorption of the lead" to which Kehoe refers. With a range of intake of lead from water from 0 to 0.54 mgms. per day, it is not hard to imagine the occurrence of sudden minor episodes of intoxication in a man whose diet already contains 0.606 mgms. of lead per day.

In considering some of the details of this two-day diet, it is obvious that water is the largest single source of lead. With the revised analysis, only beef and coffee showed relatively high lead levels on a parts per million basis.

The Lead in Food (Scotland) Regulations 1961 restrict foodstuffs to a maximum content of 2.0 p.p.m. of lead, with certain specified exceptions. Williams (1958) is very critical of this 2 p.p.m. limit as representing a standard that can readily and economically be achieved without hardship to the food trade. In his opinion, it does not ensure that the amount of lead ingested per person each day would not reach a cumulative dose. He suggests that many human beings are already ingesting the maximum quantity of lead that can be taken without giving rise to manifestations of intoxication and estimates that if the lead content cannot be eliminated entirely, it must not as a general average, be permitted to exceed a quarter of the recommended limit.

The very large canning firm, whose baby foods were analysed, has recently begun to market its range of baby foods in glass jars instead of tins. In answer to a query on whether this was an attempt to reduce the lead intake of babies from canned foods being contaminated by traces of solder, their Chief Chemist (Barnes 1965) stated that the solder used in well made cans had a negligible effect. The lead content of their products was due to the minute traces of lead derived from the raw materials. The change to glass jars was, therefore, not related to considerations of lead content. He referred to the Lead in Food Regulations (1961) limit of 2 p.p.m. and stated that the results for any of their products was below 1 part per million.

The results for the baby foods have been presented giving the daily lead intake at different stages in the first three months of life. For purposes of comparison an estimate has been made of what this would represent in terms of the intake of a 70 kgm. adult. This shows an extremely unsatisfactory state of affairs. We cannot believe that quantities

of lead which in the adult would represent some 4 mg. per day are a safe and suitable intake for a baby under three months of age.

These calculations are influenced, however, mainly by the analysis of a single can of condensed milk. Fairhall (1937) in a study of129 samples of evaporated milk found no correlation between the lead content and the age of the milk (i.e., the length of time it has been in the can). His average result by a dithizone method was 0.11 p.p.m. Fairhall concluded that contamination from the tin-lead alloy solder used to seal the cans is of negligible hygienic importance. Monier Williams found no lead in a tin of unsweetened condensed milk and Schroeder included one tin of milk with a lead content of 0.05 p.p.m. in his series.

The essential factor in regard to absorption of lead from milk is whether or not the milk of itself reduces the amount of lead absorption. This point, which has been accepted as definite for many years, is now under some dispute.

Legge and Goadby (1912) described feeding experiments in which 2 kgm. animals were given 0.1 G. lead nitrate per day. One animal was given this dose in water and died in four months from encephalopathy. The other was given the dose in milk and had no symptoms whatever. These authors believed that the milk prevented the absorption of the lead because the albuminised substances in the milk precipitated the soluble lead nitrate.

Hunter (1957) considered the effect of milk to be based on its high calcium content. He gives a graph to demonstrate the fall in the excretion of lead produced by milk and also by calcium lactate contrasted with a rise in the output of lead in the urine when ammonium chloride or phosphoric acid are administered.

However, three speakers recently, in a discussion on lead poisoning in shipbreaking, McCallum (1963), have stated very clearly that they do not think the free issue of milk to industrial workers should be continued as this does not prevent lead poisoning.

Tompsett (1939) gave a striking demonstration that milk interferes with the absorption of lead from the gastro-intestinal tract. Adding lead in various proportions to standardised diets in mice, he showed clearly that on a high calcium diet the absorption of lead was small and was not influenced to any great extent by the amount of lead administered. There was a large absorption of lead on a low calcium diet and this was dependent on the amount administered. These observations are of importance in relation to the studies to be described later. To appreciate the degree of this effect, it is necessary to study some of the detailed figures of Tompsett's experiments.

Lead absorption in mice with varying calcium intake
(From Tompsett 1939)

Daily lead addition to diet for 14 days in Mg/day	0.05	0.1	0.50	1.0
Low calcium diet (average of four mice) Mg/100 gm.	0.457	0.856	1.76	2.63
High calcium diet (average of four mice)	0.197	0.247	0.241	0.267
Low calcium diet + added calcium glycerophosphate (two mice)	0.125	0.136	0.122	0.162

This is a very considerable inhibition of absorption.

With industrial poisoning from <u>inhalation</u> of lead dust and fume, milk or calcium will increase the storage of lead in the bones to the detriment of its elimination from the body altogether. It is thus only a temporary expedient for immobilising unbound lead which is free in the circulation. With lead <u>ingested</u>

on the other hand, there is good evidence that the presence of milk prevents the actual absorption of lead and this is obviously more important than any question of delay in its excretion. We must presume that small babies are protected to some extent from the lead in their milk by its calcium content.

SECTION IV

Clinical Observations

Industrial Exposure.

Experience of this has been very limited as there are no major lead using industries in the practice area. The cases of this type, however, serve as a comparison with the non-industrial ones which will be described subsequently.

The first patient presented with pain in the right loin and vomiting+ was diagnosed by a colleague as suffering from pyelitis. The true nature of the ailment and also the man's occupation were revealed by routine urine test for coproporphyrin which was being carried out at that time on all samples of urine received in the practice.

CASE 1. R.K., age 32, Male.

Occupational history "burner" - oxyacetylene cutter for eight years, working with scrap metal. In February 1962, he moved to shipbreaking work, but soon asked for a transfer from this because he had doubts about its effects on his health. In April 1962, he began work on railway bridge demolition.
Past Medical History - A peptic ulcer was diagnosed by X-ray in 1953. A barium meal in 1962 showed a duodenal ulcer and he was off work for five weeks because of this.
Immediate Past History - He had experienced recurring abdominal pain for two weeks and had been troubled with flatulence for a few weeks. He said that he had kept off alcohol for five weeks because he thought that his ulcer was starting up again. On 16/12/62, he developed a severe abdominal pain which he described as being in the right renal angle, and began vomiting. He was seen by a colleague who diagnosed a pyelitis and started treatment with Sulphadimidine. On 17/12/62, the pain was still present and on further enquiry he described it as radiating from the umbilicus round to his right loin. He had vomited six times

and had been constipated for the previous two days. He had no pyrexia, dysuria or frequency. Examination of the abdomen was not helpful. He had some tenderness in the right renal angle. This man was a visitor to the town and an occupational history was not elicited as it did not appear relevant to pain in this situation. It was observed that 24 hours treatment with Sulphonamide had effected little improvement and a urine sample was obtained.

Examination of the urine showed a heavy deposit of urates. Albumin negative, glucose negative. Coproporphyrin estimation with the Donath apparatus gave a result beyond the limit of the scale (beyond the range 3,000 to 5,000 µg/litre).

This patient was lodging in a railway house and as it was known that the disused railway bridges were being dismantled with oxyacetylene equipment it was suspected in view of this coproporphyrin test result that this would be his occupation. He was revisited and the occupational history obtained. On examination of his mouth, a well marked blue line was visible at the lingual surface of the base of the lower right fifth tooth.

Laboratory Examinations: (17/12/62)

Hb:	13.8 gm./100 ml.	W.B.C:	10,400 /cu.mm.
P.C.V:	40%	Reticulocytes:	3.1%
M.C.H.C:	34%	E.S.R:	17 mm. in 1st hour (Westergren)

Film: coarsely stippled cells present - 0.7%
Urine coproporphyrin: 6560 µg/litre.
Blood lead: 104.9 µg/100 ml. (Lab. G.)

31/12/62 - Repeat urine coproporphyrin estimation - 2402.6 µg/litre.

By 7/1/63 his condition had settled down without specific treatment and the consultant physician in Glasgow, to whose care he had been transferred, considered that he was fit for work (but not lead burning meantime.)

It is interesting to note that this man stated that he had raised the question of lead burning as a cause of his dyspepsia at the time of his barium meal in April 1962. This was discounted as a possible cause (without blood or urine examination) because he had only been working in the shipbreaking industry for about two months. He was told at the hospital that it took two years for lead effects to develop.

CASE 2. A.M., age 28, Male.

Another temporary resident in the district from the same squad of men attended on 17/1/63 complaining of pain over his right lower ribs radiating round to his back for three days. The pain was made worse by deep breathing. There was no abdominal pain, nausea, vomiting or constipation. He had no pyrexia and no night sweats. He had been confined to bed for two weeks a year previously because of Pleurisy and when he tried to emigrate had been re-x-rayed five times because of this. His weight had increased by one stone in the last year. He had been a "burner" for four months only and previously was a lorry driver. No abnormality was discovered on chest examination and as he was going home on the following day, he was referred back to his own doctor.

Urine: No Albumin or Sugar.
Coproporphyrin: 4½ Degrees on Donath Scale, (200-400 µg/litre).
Blood Film showed no punctate basophilia.

No firm diagnosis could be made with this brief contact.

Cases 1 and 2 applied for treatment as National Health Service temporary residents. There was no further contact with these demolition workers for several months. In June 1963, the foreman of the squad was approached and asked if some of his men would be prepared to provide urine samples for purposes of

comparison with the sample received from Case 1. There were four men left in the demolition gang and the oxyacetylene cutting was almost completed. After a further week in which the men were erecting fences where bridges had been removed they all left the district. All four men agreed to provide urine samples.

The four samples were tested simultaneously and the effect was very striking. Three showed a vivid pink fluorescence, reading 6 on the Donath Scale (800 to 1,600 µg/litre), and the remaining sample showed no pink fluorescence (0 to 50 µg/litre) 1 Degree on the Donath Scale. When further enquiries were made it was found that the last sample had been provided by the foreman who was engaged on administrative duties and the other three had been provided by the oxyacetylene cutters.

CASE 3. J.M., age 43, Male.

This was one of the three men from the demolition squad whose urine had been found to contain a high amount of coproporphyrin. He attended the surgery three days later and asked for treatment on account of diarrhoea.

Occupational History - He had been a "burner" for one year and then had been off that kind of work for ten years, working on a farm. He restarted demolition work six months before, but insisted that at that time he was only cutting bare unpainted metal. He joined the bridge demolition team only six weeks previously. In discussion, on the manner in which he carried out his work, it was noted that because of the position of the disused railway relative to the road, the men were standing down-wind from the metal they were cutting. The mobile crane which was being used was loading lorries on the lee side of the bridge, and the bridge was gradually dismantled towards the road.

The high sides of the bridge may have had a funnelling effect on the wind. This man admitted that at times he was bending over with his head eighteen inches from the point where he was cutting the metal.

Laboratory Examinations:

Hb:	13.8 gm./100 ml.	E.S.R:	10 mm. in 1st hour (Westergren).
P.C.V:	43%		
M.C.H.C:	32%	W.B.C:	5,900 /cu.mm.

Film: Less than 0.1% stippled cells seen.
Blood Lead: 102.31 µg/100 gm. (Lab.G.)
Urine Lead: 180 µg/litre.
Urine Coproporphyrin: 757.3 µg/24 hours (after being sent to Glasgow by post).

Treatment: A simple chalk and opium mixture. Off work. Two days later, he was still feeling weak and rather shaky when he walked about. He returned a stool sample jar, which had been issued, empty, as the diarrhoea had been followed by constipation. After a further two days he was very much better and was leaving the district to return to his former farm working job.

The other two members of this demolition squad who showed high coproporphyrin results were offered advice and further investigation, but did not take advantage of this offer.

CASE 4. K.A., age 26, Male.

This young master painter asked for advice because, though he felt fit, he had lost between nine and ten pounds in weight during the course of a year. He was not aware of these studies on lead, but volunteered the information that he used white lead for priming coats, but was particularly careful in cleaning his hands after using this. When he was asked why he mentioned this, it was discovered that he had been well drilled as an apprentice on hygiene after using lead paint. His employer apparently had a father in the same trade who had died of plumbism.

On further enquiry, it was discovered that though he was very careful in his use of lead based primers he had been "burning off" lead paint with a Butane gas blowlamp. He had been shielding the blowlamp with his body and jacket to keep the wind off the surface when stripping doors. This made the work faster. He had been working at least eight hours a day and up to twelve hours a day, burning off paint most of the time, for a month. He was working his way along the outside paintwork of a housing estate, with an apprentice following and rubbing down the work after him. This method of screening the blowlamp meant that his head was often above the flame. He said that it made him feel sick and that it upset all the other painters too. - "Nobody likes doing it". It was apparently quite accepted among the painters in this area that nausea and anorexia could be expected after they had been burning in this fashion. It was realised that this was caused by the fumes, but it was not appreciated that the fumes might contain anything as toxic as lead. On having this possibility explained, the patient readily undertook to try to construct a simple metal windshield for his blowtorch.

Investigations:

Physical examination - No abnormal findings.
X-ray chest - Negative.
Urine - Albumin: Nil, Glucose: Nil.
Coproporphyrin - 3 Degrees on Donath Scale (100 to 200 µg/litre).

Haematological examination:

Hb:	15.0 gm./100 ml.	E.S.R.	3 mm. in 1st hour (Westergren)
P.C.V:	43%		
M.C.H.C:	35%	W.B.C:	5,300 /cu.mm.

Film: No stippled cells seen.

Blood lead estimation was not available at this time.

This man, therefore, had a marked weight loss which is one of the early symptoms of lead poisoning

described in the section on symptoms and signs. He was working in a trade which had given many cases of lead poisoning in the past. He had neither anaemia nor punctate basophilia. His urine coproporphyrin result was at the level which has been found in 10 per cent. of men not exposed to lead but, as already described, is also found associated with early toxic features. It, therefore, supports the possibility that the weight loss might be due to lead but gives no definite confirmation of this.

The Calor Gas Company expect a maximum working temperature of 1,300°C. from their Butane blow-torches under ideal working conditions. This can be compared with the working temperature of the paraffin blow lamp at 1,100°C, and of the oxyacetylene apparatus which operates at 3,500°C. The hazard from lead fume is greatly increased with the very high temperature blow-torches but there is no question that lead can be volatilised at 1,300°C.

From experiments with this type of "Calor Gas" blowtorch at the Manchester University Department of Occupational Health, however, King (1965) has found that virtually no lead is volatilised with application of heat sufficient to melt paint. This only occurs if the heating is sufficiently prolonged to char the wood underneath. The lead hazard in this particular process is in the rubbing down of the wood after scraping and much of this would be borne by the apprentice who followed after this man.

The nausea and anorexia which he described seem most likely to have been due to the fumes of the volatile oils such as turpentine which would be created by the blow-torch, rather than to lead. The anorexia would in turn result in weight loss. This illustrates that even in a trade where lead poisoning has been

known to occur, early symptoms associated with plumbism must not be accepted uncritically. The diagnosis may present many difficulties.

The last industrial case was seen in another area with the patient's family doctor who had made a clinical diagnosis of lead poisoning. My colleague willingly agreed to a urine sample being tested on the Donath apparatus and compared with the lead estimations which would be done when he was referred to hospital.

CASE 5. J.McR., age 42, Male.

Previous occupational history: Oxyacetylene burner with the National Coal Board for ten years cutting unpainted metal. Shipbreaking for two years, three months. For the first part of that time he was cutting up tankers, but for nine months prior to February 1964, was engaged in breaking up warships. There were apparently four men using oxyacetylene cutting apparatus on the ships and several other workers cutting down the sections to smaller pieces on the shore. There was never any rotation of the workers between these jobs. Two of the three other men working on the ships had been diagnosed as suffering from lead poisoning by the appointed factory doctor who was also the Works Medical Officer and were not infrequently taken off work for two weeks at a time. One of them was off work every two months for this reason.

Medical examination was described by the patient as occurring fortnightly while he was working on the warships. It consisted of inspection of teeth and eyes, and a question on how the man was keeping. Occasionally haemoglobin estimations were done but this only occurred once with this patient in the time he worked with this firm (two years, three months). The patient persistently complained of a burning feeling in his abdomen but the works doctor said that was just indigestion, though indigestion tablets provided by

his family doctor had no effect. He was provided with a mask at work and said that he used this, but the mask was labelled "for dust only" (Siebe Gorman Mark VIII Respirator).

He described the amount of dust and vapour which was created when using his burner below deck as being very unpleasant indeed. He was diagnosed by the family doctor on 10/2/64 as suffering from lead poisoning on a basis of his occupation, the blue line on his gums, colicky abdominal pains and a weakness of grip of his right hand and wrist. He also complained of anorexia, insomnia and a burning discomfort in his epigastrium after food and after lifting heavy weights. He had alteration in his bowel habits, having become constipated, for two to three days at a time, instead of his former usual daily motion. He was tired to an excessive degree and found that he was short of breath on climbing a hill and had to stop because of this. He also complained of numbness and tingling in his fingers which went very white. A urine sample tested on the Donath apparatus gave a reading of 6 (800-1600 µg/litre).

He was seen at a hospital out-patient clinic where a senior medical registrar noted that he had a blue line, his haemoglobin was 71%, he showed slight basophilic stippling, and in view of the raised urine coproporphyrin agreed that it seemed as if he had lead poisoning, but commented that his abdominal pain sounded more like that of an ulcer. A barium meal was arranged prior to his admission for further investigation. The letter dated 2nd March, apologised for the delay in writing, but this was because the "serum lead" report had not yet come to hand. On 9th March 1964, the "serum lead" was reported as 105 µg.%. The comment was made "this is not significantly raised and therefore does not confirm that he is suffering from lead poisoning".

20/4/64.- There had been some delay over the barium meal which was reported as showing slight deformity of duodenal cap, but no ulcer, and there was a promise of a hospital admission the following week for further investigation.

On 13/5/64, the patient's haemoglobin was now 85%, he had no punctate basophilia and no blue line. A maximum histamine test meal showed a fairly normal acid and a second "serum lead" result had not yet been received. A 24-hour urine coproporphyrin excretion was recorded as 1480 µg. The opinion of the senior registrar on this case was "All things considered I do not think this man's symptoms are due to lead poisoning. I think he has a small duodenal ulcer, but I do not think there is any indication for further treatment".

A copy of this opinion was forwarded from the hospital to the Ministry of National Insurance. The Medical Board under the National Insurance (Industrial Injuries) Acts, had deferred a decision on whether this man suffered from lead poisoning until they received this report. They completed their proceedings on 18/5/64 in the light of this report concluding that this man did not suffer from lead poisoning.

On 19/5/64 his "serum lead" was reported as 26 µg.% and therefore within normal limits. 18/6/64 - he was reviewed at the hospital clinic, was still complaining of epigastric discomfort, and also of tingling in the fingers. An x-ray of cervical spine showed some osteoarthritis which was presumed to be responsible for his paraesthesia. His haemoglobin was now over 100% and he had no punctate basophilia.

On 30/6/64, the report of a third "serum lead" was given as 10.5 µg.%. An appeal was presented to the Medical Appeals Tribunal against the verdict of the Medical Board that no lead poisoning existed.

This appeal was held on 20/7/64 and the Appeal Tribunal considered that the balance pointed to the claimant having suffered from lead poisoning.

Comment on this case:

The considered opinion of the hospital registrar that this man did not have lead poisoning was very unfortunate. It appears to be based on the impression, that because the patient complained of burning epigastric pain and of paraesthesia in the hands he could not have lead poisoning. All the other features of the case, however, point overwhelmingly to the opposite conclusion. The danger of his occupation is well known and is demonstrated by the fact that two of his three workmates were already poisoned. He had a marked blue line, colicky abdominal pains, weakness of his right hand, a pronounced anaemia, a greatly raised urine coproporphyrin excretion, and a blood lead level which few people would describe as "not significantly raised". To complete the picture, punctate basophilia was recorded though no precise count is given or description of the method used in examining for this. It is difficult to see what further evidence would be required.

The lack of familiarity of the senior registrar with this subject is perhaps most clearly shown by the repeated use of the phrase "serum lead". Since 90 per cent. of the lead is now accepted as being carried in the red cells (Stewart and Stolman 1960), a "serum" lead of 105 mgm./100 ml. would represent an incredibly high blood lead figure.

The progress of the case with disappearance of punctate basophilia and blue line, and fall of what must be presumed to be blood lead level from 105 mgm. to 26 mgm. and latterly to 10.5 µg/100 ml. was very satisfactory. A rise in haemoglobin from 71 per cent. to 85 per cent. and finally 100 per cent. was a

consequence of the stopping of this lead exposure. The result of the urine coproporphyrin test by the Donath apparatus was telephoned to the patient's doctor the morning after receipt of the sample on 11th February whereas the blood lead result was not available until 9th March. This simpler and much more rapid procedure was therefore of great value. It is interesting to note that three months later a similar grossly abnormal result was obtained by the hospital. No further urine coproporphyrin tests were done for another six months but by that time a Donath reading of 2 (50-100 µg./litre) was obtained.

Discussion on Industrial Cases.

These cases show a number of the difficulties in diagnosis in cases of frank lead poisoning where this would be expected to be most easy.

The first case was mis-diagnosed completely on clinical grounds and the credit for the diagnosis rests entirely on the routine screening test with the Donath apparatus. The co-existence of a duodenal ulcer and frank industrial lead poisoning are noteworthy. The condition settled down, however, without the need for specific treatment such as chelating agents.

The second patient had a urine coproporphyrin level in the zone which Donath originally regarded as suspicious, but the remaining three lead burners in the team had urine coproporphyrin levels of the order which Donath regarded as indicative of frank industrial poisoning, and in one of these cases this was confirmed by blood and urine lead levels, though the punctate basophil count was normal.

The young painter said that he was not aware that the use of a blowlamp could cause lead fume from which he could be poisoned. He was obviously unfamiliar with the leaflet on Lead Paint precautions

prepared by H.M. Factory Inspectorate under the Lead Paint Regulations of 1927. This states quite clearly that painters engaged in burning off multiple coats of old paint from structural steelwork by means of blow-lamps have developed lead poisoning from fumes. Employers are obliged to issue a copy of this leaflet annually to all men using lead paint, but this painter had never seen this leaflet.

The last case shows the number of disturbing features. The most notable of these was the difficulty in obtaining confirmation of the general practitioner's diagnosis of lead poisoning. I can only presume this was due to the unfamiliarity of the doctor in hospital with the subject. If the story is true that one of the other men on the job was taken off work for two weeks every two months because of diagnosed lead poisoning, then it seems that he should certainly have been kept off longer. Hunter (1957) suggests three months.

The legal aspects relating to these various occupations are very interesting. New regulations under the Factory Acts were published in 1964 by the Ministry of Labour, requiring the estimation of the haemoglobin content of the blood at three monthly intervals for workers exposed to hazards from lead. These new regulations, however, do not apply to all persons exposed to lead hazards, but only to those whose hazard was already covered by specific regulations. The 1964 regulations and previous ones apparently do not cover bridge demolition and shipbreaking to an adequate degree. The Factory Act of 1961 which is a consolidating Act states in Section 126, that the Minister has power to make regulations governing the repair or breaking up of a ship in a basin, a harbour, or a wet dock, but no such regulations have been made. The requirements for the

removal of dust and fume under Part 4, Section 63, do not apply to men breaking up a ship which is actually in the water, though they do apply when the sections of the ship are brought on shore to be cut into smaller pieces. Section 127 of the Factory Act, dealing with building operations and works of engineering construction, includes bridges, and again the Minister has power to make regulations, but regulation 20 of the Construction (General Provisions) Regulations (1961) covers grinding, spraying, or manipulation, but not demolition, as requiring ventilation or respirators. The special regulation concerned with demolition (Regulation 41) does not deal with dust and fume.

From the annual report of H.M. Chief Inspector of Factories on Industrial Health (1963), it can be seen that shipbreaking annually provides a quota of patients with lead poisoning. The number has fallen from fifteen out of a total of sixty-four notified cases in the whole of the country in 1959 to five out of a total of ninety-three notified cases in 1963. With such a well known cause of lead poisoning it seems strange that the Regulations do not ensure the maximum protection for the worker. The same annual report mentions four cases of lead poisoning having been notified in men demolishing railway bridges as part of various modernisation schemes, but these are not included in the total figures given for the year as such work on railway bridges is excluded from the provisions of the Factories Act.

It would seem that there is a great need for regulations governing the use of high temperature blow-torches on painted metal surfaces in any situation. These should require preventive measures against dust and fume, periodic medical examinations, and notification in case of poisoning. This would deal with men working in enclosed areas in ships who are frequently exposed to

very high concentrations of lead fume (McCallum 1963) and also small groups of workmen engaged in demolition who are at present unsupervised. With the continuing closure of railway lines, there must be a great number of disused railway bridges still awaiting demolition.

Screening of Patients for Evidence of Increased Lead Absorption

Punctate Basophilia.

When the plumbo-solvent tendencies of the water supplies were appreciated, blood films were sent to Peel Hospital Laboratory from thirty-eight cases of gastro-enteritis for search for Punctate Basophilia. This was present in twenty-seven (71 per cent.) but the range of "stippled cells" was from less than 0.1 per cent. to 2 per cent. of red blood cells. This seemed of little diagnostic value in relation to an acute gastro-enteritis, because in an area where the water supplies contained an unusual amount of lead, some persons might have been expected to have small numbers of stippled cells in the blood without symptoms of any kind. The significance of a finding of Punctate Basophilia in a blood film in this community was explored by submitting blood films for Punctate Basophil count on every occasion subsequently on which blood samples were taken from any patient for any examination. The films were stained with Alkaline Methylene Blue and examined by indirect light by the Consultant Pathologist. In all, blood films were examined from 450 of the 2,042 patients in the practice between January 1961 and May 1963.

TABLE 20

Examination of Blood Films for Punctate Basophilia

Total of all blood examinations:	450 persons
No Punctate Basophilia reported:	381 "
Punctate Basophilia reported:	69 "

Of these 69 patients, 59 had one or more of the following complaints of gastro-intestinal disturbance: abdominal pain, vomiting, diarrhoea and flatulent abdominal distension. This is a very high

proportion of the relatively small number of positive findings. In four of the remaining ten patients, there was an obvious reason for the presence of stippled cells.

TABLE 21

Punctate Basophilia without Gastro-intestinal Disturbance

	No. of Cases
Pernicious Anaemia (a normal finding in this disease)	2
Industrial Exposure	2
Maternity patients with other evidence of increased lead absorption (increase in blood lead or urine coproporphyrin)	2
Maternity patient. Previous sterility history and premature labour.	1
Bronchitis	1
Foot Drop (subsequent operation for prolapsed intervertebral disc.)	1
Rash (unknown aetiology) + chronic constipation.	1

In the light of these findings, it can be said that in the community studied, punctate basophilia occurs infrequently (13 per cent.). When it is present it is largely (88 per cent.) but not exclusively associated with symptoms of gastro-intestinal disturbance.

Urine Coproporphyrin Test.

When a Donath apparatus became available for use in the practice, a large scale screening programme was begun for glycosuria and urine coproporphyrin estimation. The patients were only informed of the first of these and since various screening campaigns for diabetes were being reported in the press there was little comment. A large number of patients attending for a wide variety of complaints were asked to provide urine samples. Over a two-year period (October 1961 to September 1963) the number of new cases of diabetes

detected was ten compared with a known incidence of ten cases at the beginning.

TABLE 22

Use of Industrial Coproporphyrin Screening Test in General Practice

October 1961 to September 1963

Total Number of persons	Total Number of Urine Samples	Donath readings 3 and above (100-200 µg/litre range and above)	
		Patients	Samples
746	1,858	104	177

Six of the patients had known industrial exposure to lead. If they are subtracted, then the proportion of patients showing Donath scale readings of 3 and above was 12 per cent. When the records of the 104 patients were studied, however, it was found that a large proportion had one or more of the symptoms of gastro-intestinal disturbance mentioned in connection with punctate basophilia.

TABLE 23

Conditions associated with Raised Urine Coproporphyrin Excretion

	Patients	Urine Samples
1. Known hepatic or biliary tract disorder	8	18
2. Industrial exposure to lead fume	6	8
3. Pregnancy	21	48
4. Gastro-intestinal disturbance other than in the above cases	52	86
5. Other Conditions (including some vertigo cases)	17	17
	104	177

Hepatic disorders are known to give raised urinary coproporphyrin excretion and the raised levels in the cases of industrial exposure from oxyacetylene cutting of disused railway bridges were very marked. While it is tempting to consider that the number of maternity patients showing this level (22 per cent. of the total) might be an illustration of the sensitivity of this group to increased lead intake, it must be stated that the maternity patients studied throughout their pregnancies had an average of 7.5 urine samples per patient, compared with the average of 1.7 urine samples per patient for all the others. More detailed results for maternity patients will be described later.

Only 2 per cent. of all patients studied, had urine samples containing coproporphyrin at this level (Donath reading 3 or more) and did not come into the four main categories specified. This must be compared with the observation of Zielhuis(1961) that 10 per cent. of normal male workers in industry with no exposure to lead would show this level of urine coproporphyrin excretion.

We may summarise that only 12 per cent. of patients showed urine coproporphyrin levels of Donath Degree 3 (100-200 µg/litre) or above. If we exclude the hepatic and industrial cases, and also pregnancies which were much more intensively studied, this is reduced to 11 per cent. of whom three out of four had symptoms of gastro-intestinal disturbance.

This, therefore, enables us to assess the degree of exposure to lead in a part of the population by two different industrial screening methods. With both tests about 11 or 12 per cent. of the patients were found to differ from the rest and a high proportion of such patients had symptoms of gastro-intestinal disturbance. We are dealing for the most part with

the earliest detectable signs of Physiological disturbance rather than with "poisoning" in the industrial sense, though cases showing punctate basophilia of the order of 0.6 per cent. might be considered to warrant investigation if they occurred in industry. However, levels of lead intake which might be within the accepted range of tolerance for the adult male in industry are not necessarily safe for the young child, the pregnant woman, and especially the foetus in utere.

Further observations on the use of a Urine Coproporphyrin Screening Test

Donath (1956) warned that coproporphyrin is easily changed by light and for the collection of 24-hour samples of urine it is therefore advisable to use dark coloured bottles. He suggested the addition of thymol as a preservative for 24-hour samples, but I have not found this to be reliable. Haeger-Aronson (1960) suggested adjustment of pH by the addition of sodium carbonate (5 g. to 1 litre) and this is more effective when a preservative is required.

All the urine samples described in these studies were tested with the Donath apparatus on the day on which they were passed. They were collected in dark coloured bottles and no preservative was used. It was not possible to test these samples whenever they were received because though the test takes only a little over ten minutes the number involved was considerable. They were, therefore, left for testing each evening after the evening surgery was finished. Two studies were made in an attempt to estimate the loss of coproporphyrin which resulted from this delay in performing the test.

In the first of these sixty-seven urine samples from ante-natal maternity patients attending the Simpson Memorial Maternity Pavilion were tested

in the clinic immediately after the samples had been provided and the test was repeated after the samples had been kept in dark bottles for six hours. Using the method advocated by Zielhuis(1961) of calculating an average of the results according to the Donath scale, the samples when fresh had an average coproporphyrin content of 1.13 and six hours later an average of 1.06. The use of two places of decimals in this fashion is quite unjustified in relation to the sensitivity of the test and the number of patients involved. It is used here purely to demonstrate the difference. For all other purposes it would be much more appropriate to quote the averages to one decimal place.

A similar study was undertaken with forty long stay mental patients at Dingleton Mental Hospital, Melrose. These were men who had been living for a number of years on a water supply which was discovered to be plumbo-solvent. Though forty samples were obtained four were found to be insufficient in quantity for the test to be repeated after an interval. Of the remaining thirty-six samples the average result in Donath units when tested fresh was 1.2 and twelve hours later when these samples were tested again the average remained 1.2. Apprehension that an appreciable loss of coproporphyrin might result from delay in testing of the samples would, therefore, seem unjustified if samples are tested within twelve hours.

Most of the results in my studies have been Donath scale readings 3 and below, whereas the originator of the apparatus (Donath 1956) was concerned more with industrial cases giving readings 4 and above. An attempt was, therefore, made to check the effectiveness of the Donath instrument in the lower ranges (Frazer 1964). The Donath test cannot be done with pure solutions but only with urine. Mesoporphyrin

was therefore added in the range 20 to 700 µg./litre to urine which gave a Donath reading of less than 1.

TABLE 24

Comparison of Mesoporphyrin Fluorescence with Donath Scale

Actual Mesoporphyrin Concentration (µg./litre)	Donath reading (units)	Donath's stated equivalence for Coproporphyrin
0	less than 1	0
20	less than 1	0
35	less than 1	0
70	1	0-50
150	2	50-100
250	3	100-200
425	3	100-200
550	4	200-400
700	about 4.5	about 500-600 (?)

Mesoporphyrin, according to Frazer, may give less fluorescence, weight for weight than coproporphyrin, but even allowing for this it appears that the apparatus may tend to underestimate rather than overestimate.

Urine Coproporphyrin Excretion of Mental Patients.

It was noted that certain patients whom Davidson, et.al. (1933) found difficulty in diagnosing as suffering from plumbism were admitted to a mental hospital in the course of their illnesses. It seemed therefore that the screening of new admissions to a psychiatric hospital might serve as a rapid method of assessing the possibilities of increased exposure to lead over a wide area. The Medical Superintendent of Dingleton Mental Hospital, Melrose, agreed that his staff should provide urine samples from all patients within the first week of admission for testing on the Donath apparatus. Samples were obtained from 119 patients during seven months in the winter of 1963-64.

The average of these results on the Donath scale was 1.8 and this was considerably higher than that obtained from the 40 long stay patients mentioned previously (1.2).

It had been realised that some of the drugs used in the treatment of the psychiatric patient might have hepato-toxic effects and this might give misleading results with the Donath apparatus. When the twenty-six cases who gave Donath readings of 3 or above were studied, it was found that their homes were scattered very evenly throughout the Borders. No particular area provided any great number of high results. Patients with alcoholism, however, showed very prominently. Seven of the twelve male patients showing coproporphyrin results above 3 on the Donath scale came into this category and two female patients who gave Donath results of 6 (800-1600 µg./litre) had been admitted for treatment of alcoholism. Urine lead estimation on these two patients were 47.5 µg./litre (40.31 µg./24 hours) and 52.5 µg./litre (45.68 µg./24 hours) (Lab.G.). Though not raised to a level which would be considered significant in industry, these results are both above the normal range for this laboratory (23.3 ± 12.5 µg./litre).

The association between the intake of alcohol and an increase in urine coproporphyrin excretion is well known. Sutherland and Watson (1951) comment that in chronic alcoholics there is a marked variation in the time taken for return to normal results after the cessation of drinking.

Diarrhoea as a possible cause of Porphyrinuria.

An attempt was made to confirm that diarrhoea in itself did not upset the porphyrin metabolism. Urine samples were obtained from patients with diarrhoea from the Edinburgh City Infectious Diseases Hospital.

These, along with specimens obtained in the practice, give a total of fifty-four urine samples from forty-four patients with diarrhoea of known cause. All the results were in the ranges below 100 µg./litre.

TABLE 25

Urine Coproporphyrin Excretion in Diarrhoea of Known Cause

Infectious Diseases Hospital Cases	Patients	Urine Specimens
Dysentery: Sonne and Flexner	9	10
B. coli Enteritis (0119 and 026)	12	12
Paratyphoid B.	5	5
Typhoid	2	2
Practice Cases		
Sonne Dysentery	10	15
Non-Paralytic Poliomyelitis	2	5
Immunisation Diarrhoea (Oral Poliomyelitis vaccine)	2	3
Colchicine Diarrhoea	1	1
Thyrotoxic Diarrhoea	1	1
	44	54

All were in the range 0-100 µg./litre
(50 in range 0-50 µg./litre
4 in range 50-100 µg./litre)

From this small series, there was no evidence that these diarrhoeas produced a rise in urine coproporphyrin output. One case which was studied after this series had been completed, however, had a result in conflict with these.

This was a Boy Scout camping at Farm B, whose unsatisfactory water supply has already been described. This boy developed diarrhoea which settled rapidly on treatment with chalk and opium mixture B.P.C. and a urine sample gave a Donath reading of 4 (200-400 µg./litre).

On stool culture, however, Shigella Sonnei was isolated. A urine sample (24-hours) 1150 ml. in volume, was reported as having a total lead content of only 15 µg. (Lab.N.) Though he was using a very undesirable water supply, it seems possible that he was passing a highly concentrated urine as the result of the fluid loss from his diarrhoea, and that this may have influenced his urine coproporphyrin result.

A second case, a male aged 58, had gross blood loss from a duodenal ulcer (Hb 63 per cent.) and his maximum Donath reading was 4 (200-400 µg./litre). Punctate basophils were observed in his blood film, but less than 0.1 per cent. Blood lead estimation was 55 µg./100 ml. (Lab.P.). This man died from a post operative Ileus following a gastro-enterostomy and at post mortem he was found to have a marked necrotising enteritis with Cl. welchii cultured from the necrotic jejunal loop. A full series of tissue lead analyses was obtained from this patient and these were all within normal limits.

TABLE 26

Tissue lead analyses in a patient with previous raised urinary coproporphyrin excretion.

Tissue	Lead (mgm./100 g.) fresh tissue (Lab.N.) *
Liver	0.05
Kidney	0.015
Brain	0.017
Rib	0.32
Vertebra	0.32
Femur	0.83

Larson and Watson (1949) have found no evidence in humans or experimental animals (dogs) of absorption of coproporphyrin from the gut and its excretion in the urine either with ingested blood or raw meat or with spontaneous gastro-intestinal haemorrhage.

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* Lab.N. - Northern General Hospital Laboratory, Edinburgh.

In this patient the urine coproporphyrin level would have been considered by Donath (1956) to be suspicious, and by Zielhuis (1961) to be associated with increased lead absorption. The blood lead level is raised according to Kehoe's (1961) normal figures, but not to the level of industrial toxicity and the punctate basophil count is not significant. The picture is completed by the series of tissue lead analyses with its normal values.

Only one patient of the 740 in the practice who had no industrial exposure, showed regular urine coproporphyrin readings in the range which would be associated with industrial hazard. This female patient, aged 50, over a period of a year from March 1963 to March 1964 had seven different readings of 5 on the Donath scale (400-800 µg./litre) and two of 6 (800-1600 µg./litre). Very occasional punctate basophil cells were seen on one of four occasions on which blood films were examined. Blood lead estimations were 20.8 µg./100 g. and 48.7 µg./100 g. (Lab.G.). This last result is outside the normal range for the laboratory concerned, but does not match the blood lead results of industrial cases showing similar coproporphyrin levels. She had no anaemia (Haemoglobin 15.6 g./100 ml.). She suffered from intermittent flatulence, dyspepsia and constipation and occasional bouts of vomiting. She did not have an excessive intake of water and tea. She discontinued her practice of filling the kettle at the hot tap at the beginning of the year over which these observations were made and a single water sample from her house showed no lead. She had no industrial lead exposure, she had no history of excessive intake of alcohol. A transaminase estimation done at Peel Hospital was reported as normal, but this was the only test of liver function performed.

While this patient's continued raised urine coproporphyrin in association with a slightly raised blood lead level suggested the possibility of chronic lead poisoning, the source of this was not easy to identify.

Before the analyses of the lead content of foodstuffs already described, it was presumed that this patient's water supply must have at times a high lead content and this had escaped detection by the single sample which was taken. It now seems much more probable that her diet may have contained an excess of some of the items which were demonstrated to contain increased amounts of lead.

With some patients the rise in urine coproporphyrin level associated with gastro-intestinal disturbance was not immediate. This point was studied by testing daily urine samples from a small boy aged six after an attack of diarrhoea and vomiting.

TABLE 27

Fluctuation in Urine Coproporphyrin Level after Gastro-Enteritis

Nov.29 - Onset of illness	Nov.30,	Dec.1,	2,	3,	4,	5,	6,	7,	8,	9,	10,	11,	12,	13
Donath Results:	1	1	3½	3	3½	2½	3½	2½	1	1½	2	1	2	

This boy showed a rise in urine coproporphyrin between the fifth and the tenth day after his acute gastro-enteritis by which time any question of dehydration from his very brief attack was long since past.

Gastro-intestinal Disorders.

In the area of this study, there has been prevalent a type of gastro-intestinal illness which occurs in single cases, in groups, or in epidemic form. Its features are abdominal pain and nausea, with vomiting and/or diarrhoea. There is frequently also eructation, flatus and distension of the abdomen. There is no pyrexia and no rise in White Blood Count or Erythrocyte Sedimentation Rate. The duration is often less than twenty-four hours, although it may last for several days. The illness may affect one or more (often several) persons in a household and can occur repeatedly in the same person, recurrence in some cases being separated by only a few days. Onset and termination of vomiting and diarrhoea are abrupt. In some families it seems that those who vomit most have less diarrhoea and vice-versa. Many patients have returned stool sample jars after two or three days without having been able to provide the specimen requested, because the diarrhoea was followed by a period of constipation.

Cases have occurred simultaneously in isolated localities at opposite ends of the practice. Lists of foods eaten, compiled both by the family doctor and by the staff of the Public Health Department, have been completely unhelpful. Bottle fed babies have sometimes been affected at the same time as adults. Some affected patients have said their dogs also had diarrhoea.

A good description of detailed symptoms was obtained from a doctor not in general practice, who has suffered from this ailment a number of times: there is an initial malaise followed by abdominal unrest as if diarrhoea is going to follow but diarrhoea does not necessarily occur. Tea and coffee then produce nausea.

There is a metallic taste in the mouth. The malaise is followed by lethargy and flatulent distension of the abdomen. There is considerable passage of flatus per rectum. Sharp stabbing abdominal pains occur and are quite often in the Right Iliac Fossa. There is sometimes aching in the back of the legs and occasional aching of the eyes. On occasions this doctor was conscious of a vague stiffness in the muscles of his neck but this did not occur every time.

A trained nurse whose bad water supply has already been mentioned (House "L") had a large number of attacks of this sort among her family, and these ceased abruptly when she began using water for cooking and drinking brought from the city thirty miles away. She described one such episode in a child of three and a half: He passed an unusual amount of flatus during the afternoon. Around 4.30 p.m. he became very irritable and listless, and was put to bed shortly after 5 p.m. He passed two normal stools while being prepared for bed and complained of abdominal pain. At 10 p.m. he awakened crying with pain but settled down quite quickly again. Next morning at 5 o'clock, he awakened suddenly, passed much flatus smelling strongly of rotten eggs, and then vomited. He began crying with abdominal pain, but this was relieved by passing a large loose stool. He slept till 8 a.m. when he had abdominal pain, vomit and diarrhoea, and then slept till 10 a.m. when he appeared to be quite recovered.

An example of a more prolonged attack affecting a girl aged six.

September 7, 1960 - Abdominal pain, vomiting and diarrhoea, she then seemed quite well until:

September 11th - three loose stools,

September 12th - two loose motions in the forenoon, diarrhoea every fifteen minutes for 2½ hours from 4.30 p.m. onwards.

13th - Six motions between 8 and 9 a.m.

14th - Five motions between 8 and 9 a.m. and five in an hour about noon.

15th - Two loose stools about 9 a.m. and vomited once.

Between the attacks of diarrhoea she was playing normally and not obviously unwell. She never showed any rise in temperature. Stool culture was negative.

One of various examples which impressed upon me that an association between the water supply and gastro-enteritis cases might be genuine was obtained from a page in the record of new calls kept in the practice. In the morning the water supply was noted to have a slight yellowish discolouration. New calls were received during the day from various parts of the practice for the following conditions.

Mr. R.S.	Acute retention of urine.
Mr. J.A.	Barbiturate coma.
Mr. J.M.	Diarrhoea.
Miss R.B.	Diarrhoea, vomiting and vertigo.
Mr. W.S.	Vertigo.
Child F.B.	Diarrhoea, vomiting and headache.
Mrs. J.L. (11.30 p.m.)	Acute severe abdominal colic.

Mrs. J.L. had had recurrent attacks of this type over a period of ten years. She had had a cholecystectomy and had subsequently had full hospital investigation without any cause being found. Her last attack coincided in time with a previous episode of diarrhoea and vomiting affecting Child F.B. and other members of that child's family. The meteorological records showed heavy rainfall four days prior to each of these two episodes.

The population accept this ailment as transient and self limiting and tend only to ask for medical treatment in cases of unusual severity or duration. It is thus very difficult to obtain a true picture of the incidence. Two patients consulted the doctor about this illness from an isolated community of sixty persons. Enquiries made by one of them revealed that eighteen others had been similarly affected about the same time. Other instances with groups less clearly defined in a geographical sense suggest a considerable incidence of this type of minor disorder.

A detailed record of the symptoms of such cases was kept for a long period in 1960-61. As well as giving the incidence and dates of onset of cases known to the doctor this gives a clearer picture of the frequency of the various symptoms. The date on which the illness was reported to the doctor was recorded along with the date of onset, the presence of the commonest symptoms (vomiting, diarrhoea, abdominal pain, unusual abdominal distension), and other complaints made by the patients.

TABLE 28.

Cases recorded in the period 29th August 1960 to 20th July 1961

Month	No.of Cases	Vomiting	Diarrhoea	Abdominal Pains	Unusual Abdominal Distension	Other Complaints				
						Pyrexia	Headache	Dizziness	Muscle Pains	Bad Taste in Mouth
1960										
Aug.	4		4				1		1	
Sept.	43	21	33	21	12	1	1	1		
Oct.	18	9	13	5	2					
Nov.	28	7	18	13	2	1	1			
Dec.	19	7	11	9	2		2		1	
1961.										
Jan.	30	13	20	22	7	1	5	6	1	1
Feb.	26	11	21	13	5			1	1	2
Mar.	27	7	14	5	1		1		1	1
Apr.	13	5	10	2		1				
May.	39	23	27	9	2		4			
June	35	12	18	9	5	1	1			
July	30	10	14	7	1	1	4			
TOTAL:	312	125	203	115	39	6	20	8	5	4

This demonstrated that diarrhoea was by far the commonest complaint reported to the doctor and that unusual abdominal distension was less frequent than had been expected. The fact that pyrexia is rarely associated with the main symptoms is well illustrated.

Correlation between Heavy Rainfall and Incidence of Cases.

The annual rainfall figures for 1961 and 1962 were obtained from a Meteorological Station twenty miles to the south in the same range of hills as the Innerleithen catchment. These were compared with the fluctuating incidence of gastro-enteritis to see if there was any justification for the patient's suggestion that this condition followed a spate. There was a strong clinical impression that this might be correct.

It was found that on five occasions, groups of six or more cases followed closely after very heavy rainfall, totalling more than 30 m.m. over a few days. All occasions on which 30 m.m. of rain fell within four days were listed between September 1960 and July 1961. A comparison was made between the number of cases reported as having onset in these periods, the number in these four days plus the two days which followed and the total of all the cases which had been noted in the month. Since this was not easy to interpret, calculations were made from the monthly totals of the number of cases which would be expected for any periods of four and six days if the cases were evenly distributed throughout the month. Where the number of cases exceeded the calculated number it has been shown in red.

TABLE 29.

Comparison of Heavy Rainfall and Case Incidence (1960-61)

Heavy Rainfall Exceeded 30 mm. over 4-day period beginning:	Rainfall exceeded 10 mm. per day on:	Cases		Monthly Total	"Calculated Expected Cases".	
		Days 1 - 4	Days 1 - 6		4 days	6 days
Sept.13	Sept.13,14	8	9	43	5.6	8.4
Nov. 1	Nov.1,2	3	8	28	3.7	6.6
Nov. 9	Nov.9,11,12	1	3	28	3.7	6.6
Nov.29*	Nov.29,30 Dec.2,3,4	2	5	19	2.4	3.6
Dec.25	Dec.25	8	11	19	2.4	3.6
Jan.3	Jan.3,5	2	5	30	3.8	5.7
Jan.26	Jan.26,29	6	13	30	3.8	5.7
Feb.5	Feb.5,6,8,9	10	11	26	3.8	5.7
Feb.25	Feb.26	7	13	26	3.8	5.7
Mar.28	Mar.28,29	5	5	27	3.5	6.0
Apr.11	Apr.11,12	0	0	13	1.7	2.5
July 12	July 12	5	7	30	3.8	5.7

The basis for the clinical impression is clearly demonstrated for on several occasions there was a marked rise in the number of cases after heavy rainfall. This increase was made more prominent because of the corresponding decrease in the rest of the month. This was shown in the extreme in February where twenty-four cases were recorded in the twelve days following two episodes of heavy rain and only two cases in the remaining sixteen days of the month.

* The clinical cases occurred in December, so December averages have been used.

It is equally obvious that no constant correlation has been shown for on some occasions, similar heavy rainfall was followed by few or no recorded cases. With a condition where the doctor may be notified of as few as two out of twenty cases, as mentioned previously, the potential errors involved are very great. There can be no definite conclusion but the grounds for suspecting an association can be better appreciated.

Bacteriology.

Methods.

Specimens of faeces from patients with diarrhoea were cultured during the period October 1958 - May 1963 in an attempt to identify a specific bacterial pathogen. Because of the suggestion of an association with boiled water, anaerobic culture for Cl. welchii was requested in addition to the routine culture for Enteric and Dysenteric organisms done by the Bacteriology Department, Edinburgh University (Cl. welchii spores can withstand boiling, the organism is frequently found in the intestine of the sheep and sheep were normally present in one of the two main catchment areas and on one occasion were also found at the other).

From 1960, detailed stool examination was undertaken as a research study by the Bacteriology Section of Peel Hospital Laboratory. This consisted of microscopic examination for Giardia and other parasites and specific culture for Shigella, Salmonella, B. coli, Staphylococci and heat resistant Cl. welchii.

Previous Experience.

A high proportion of positive results had been obtained from stool cultures in my previous urban practice of 3,000 patients in 1957 and this was a marked contrast to the results obtained after my removal in October 1958.

Previous Practice Stool Culture Results

Year	Sonne Dysentery	Salmonella	Cultures Positive	Negative
1957	63 Cases	0	63	37
1958 (Jan.-Sept.)	4 "	5 (4 strains)	9	24
			72	61

There were also 70 negative results following previous positive cultures.

Sonne Dysentery.

During the period October 1958 to May 1963, in the present practice, there were two outbreaks of Sonne Dysentery. A considerable amount of Bacteriological work on cases and contacts was needed to control these two brief episodes. The organisms, unlike those found in the previous practice, were not sensitive to sulphonamides.

1959 12 Cases - All diagnosed within three weeks.

Stool Samples:	
Positive	29
Negative	75
	104

1962 42 Cases - All diagnosed within twelve weeks.

Stool Samples:	
Positive	67
Negative	168
	235

Apart from these there were four other single cases widely separated in time during the period under study. Three of these had definitely been outside the practice area previous to the onset of illness, but the fourth had not been out of the district for several months prior to the attack, and no source of infection could be found.

Other Pathogenic Organisms.

Positive Results (Excluding Sonne Dysentery Cases).

Salmonellae	4	
Staphylococcus pyogenes	3	
Cl. welchii (Heat resistant)	2	
B. coli (026 and 0119)	8	
Candida albicans	2	
Shigella flexneri	1	(a visitor from Glasgow).
Total:	20	

The vast majority of stool samples gave negative results on culture. From October 1958 to May 1963, the total number of negative stool cultures

from patients suffering from diarrhoea, other than those listed above, was 323.

Apart from the two short periods which have been described when Sonne Dysentery was prevalent the probability of a stool sample being negative was 93 per cent. The failure to isolate a specific Bacterial Pathogen to account for this gastro-enteritis, is evident. Stool samples taken from four dogs with diarrhoea were also negative.

After this part of the study was completed, the frequency of stool sampling was reduced and more attention was paid to other aspects of the problem.

Virology.

Stool samples taken during the period 22nd February 1960 to 30th May 1963 were submitted to Virus Culture. Culture methods used were Hela cell and Monkey Kidney Tissue Culture and for a small group of patients, inoculation of suckling mice.

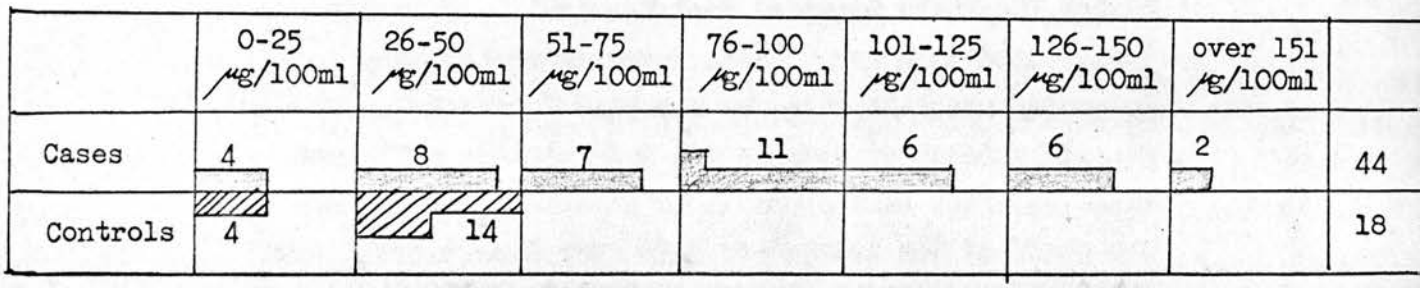
Results of Virus Culture

Positive:	
Non Paralytic Poliomyelitis (Polio virus 3):	2
Diarrhoea following Oral Polio Immunisation (Polio virus 3):	2
Coxsackie Group A9:	1
Negative:	
Patients with Diarrhoea:	143
Total Patients with Diarrhoea	148
Other Negative Results:	
Repeats of Non Paralytic Poliomyelitis:	2
Child Contacts of above	3
Total Samples:	153

These results show failure to isolate a specific pathogenic virus to account for this gastro-enteritis.

Figure 7.

Distribution of results of blood lead estimations in 44 patients with abdominal pain, vomiting and/or diarrhoea - "Cases" and 18 patients with other conditions - "Controls". (Lab. P.)



Facing page 146.

Blood Lead Estimation.

Evidence has already been given that a large proportion of those patients who were found to have punctate basophilia had symptoms of gastro-intestinal upset. A similar observation was made with the use of a urine coproporphyrin test.

The most convincing association between lead and the type of gastro-intestinal disturbance which has been described would be the demonstration of abnormal amounts of lead in the blood or urine of patients affected. With this in view, blood and urine samples were analysed for lead content by the laboratory of the Border Hospitals Group at Peel Hospital. This was facilitated by a grant for laboratory assistance, apparatus and materials for one year from the Border Hospitals Board of Management. As already mentioned, these analyses were found to be extremely difficult. The staff of the laboratory were very dissatisfied with the methods available and their ability to give accurately reproducible results, especially in the case of urine samples. There were also losses of 20 c.c. blood samples, taken during these brief acute illnesses, by laboratory accidents, such as the cracking of silica basins in the muffle furnace. These analyses were painstaking but very time-consuming.

Samples were submitted for blood lead examination in the course of investigation of certain conditions which were subsequently proved to be due to definite pathological causes other than lead. As an example, a prolapsed intervertebral disc was confirmed at operation in a case of "drop foot". Use has been made of these cases to provide a small control series for comparison with the results from patients with abdominal pain, vomiting and/or diarrhoea.

As can be seen from Fig. 7 the gastro-enteritis cases had a wide range of blood lead levels but a

considerable number exceeded 75 µg/100 ml. In contrast all in the small control series fell below 50 µg/100 ml.

A small number of the cases in Fig. 7 were provided by my colleague in the other Innerleithen practice, and others were not supported by a complete range of investigations. Details of twenty cases including both symptoms and laboratory findings are given in Table 30. This includes three married couples who had simultaneous attacks (these are bracketed). Patient G.J. (No.10) also had Rheumatoid Arthritis and his Erythrocyte Sedimentation Rate has been marked with an asterisk (*). It will be seen that for the most part Haemoglobin, White Blood Count, and Erythrocyte Sedimentation Rate are unaffected. Blood lead estimations were all done at the Border Hospitals Group Laboratory at Peel Hospital except for No.20 (J.T.) whose blood lead estimation was done at the Gardiner Institute Laboratory, Western Infirmary, Glasgow.

It was not at first realised that two or more blood lead analyses were preferable and most of the patients in Table 30, provided only a single 20 c.c. sample during the attack. Case 20 on this table had a repeat blood lead estimation four months later by the same laboratory with a result of 27.7 µg/100 ml. The history of his illness was that he had been away for a long week-end and returned home alone to an empty house. Thirty hours after his return he had a severe attack of diarrhoea and vomiting. The house had a long lead connection to the water main and he made no attempt to run this clear on his return home or when he went back to the house to make his own meals.

TABLE 30.

Symptomatology and Laboratory Findings

	Age	Sex	Abdominal Discom. or Pain	Diarrhoea	Nausea	Vomit	Flatus	Hb (gm/ 100ml.	W.B.C. (per cu.mm.)	E.S.R. mm.in 1 hr. (West)	Maximum Punctate Basophil Count	Maximum Blood Lead µg/100ml.	Stool - Intestinal Pathogens
1.M.A.	58	F	+	+	+	-	+	17.2	4,200	2	0.6%	83	None isolated
2.E.B.	62	F	+	-	+	+	+	11.7	6,500	19	< 0.1%	77	
3. J.B.	20	M		+		+		15.4	8,400	2	NIL	100	None isolated
4. J.B.	44	F	+	-	-	-	+	13.9	5,100	10	NIL	102	
5.E.C.	41	F	+	-	+	-	+	13.1	6,550		< 0.1%	130	None isolated
6.I.C.	40	M	+	-	-	-	-	14.3	4,850		NIL	111.5	None isolated
7.E.D.	24	F	+	+	+	+		12.4	5,150	3	NIL	114	None isolated
8.A.H.	41	F		+				13.1	6,350	9	NIL	74	
9.E.J.	40	F	+	+	+	+		12.2	4,700	10	0.2%	61	None isolated
10.G.J.	75	M	+	+	+	+	+	13.9	7,800	25*	NIL	96	
11.C.L.	49	F	+	-	+	+		14.9	7,500	2	NIL	37	
12.C.M.	39	F	+	+	+		+	15.7	4,900	1	NIL	13.5	
13.E.M.	25	F	+			+		13.9	5,400	5	NIL	21.5	
14.W.M.	26	M	+	-		-		15.6	5,500	1	NIL	17.0	
15.A.N.	34	F	+	-	+	-	-	12.2	7,700	8	NIL	49	
16.T.N.	36	M	+	-	+	-	+	16.8			< 0.1%	91	
17.A.P.	68	F		+	+	+	+	14.5	14,900	9	0.3%	108	None isolated
18.E.R.	21	F	+	+	-	+	+	10.5	4,500	8	< 0.1%	31	None isolated
19.J.S.	48	F	+	+	+	+	+	13.9	9,200	8	NIL	23	None isolated
20.J.T.	57	M	+	+	+	+		15.1	3,800	1	NIL	221 (Lab.G)	None isolated

A water sample taken in the forenoon when he was first seen with this illness had a lead content of 0.04 p.p.m., but no estimate can be made of the lead content of the water he had been drinking since his return home. A week of heavy rain preceded this attack.

The first patient in Table 30, M.A., female, aged 58, had a number of blood lead estimations and two separate attacks of gastro-enteritis. A blood sample taken on the day after the first attack had a lead content of 54 µg/100 ml. A week later this level had risen to 83 µg/100 ml. Two further estimations three and four months later, were 42 and 39 µg/100 ml. respectively. Stool culture in this attack was negative. A year later this patient had another similar attack of gastro-enteritis which, like the previous one, was apyrexial. On this occasion, there was no rise in blood lead content, two samples being reported as containing 41 µg/100 ml., but a Coxsackie Virus A9 was isolated from the stool. During the four week interval while the virus culture was proceeding, a barium enema was arranged, but this showed no abnormality.

Since these two patients have much lower blood lead levels later than at the time of their acute attacks it is presumed that the high levels which have been recorded are not persistent toxic levels, but rather evidence of transient increased absorption.

Discussion.

There are very many possible causes for the symptoms of gastro-intestinal upset which have been described, ranging from dietary indiscretion to malignant disease of stomach and colon. The cause of some can be diagnosed from the history, while others need Radiological and Surgical investigation. There remains in this practice, however, a large group of patients with very similar symptomatology. The type

of history is very suggestive of a gastro-intestinal irritation, rather than of an infective process and this is supported by the White Blood Counts and Erythrocyte Sedimentation Rates. The negative results on stool culture, both for bacteria and viruses, show the failure of a conventional bacteriological approach to demonstrate a cause for this. On many occasions, the stool sample container was returned unused because the diarrhoea had ceased abruptly, to be followed by two or three days of constipation.

Comparison with results from the previous practice suggests not only a different proportion of positive and negative results, but also quite a different incidence of patients complaining of abdominal pain, diarrhoea and vomiting. The number appeared to be much increased in a far smaller practice.

There is some circumstantial evidence of an association between this type of gastro-intestinal disturbance and the occurrence of heavy rainfall, but this is by no means conclusive. Evidence has also been given that heavy rainfall may increase the corrosive effect of the water supplies on metal pipes. An attempt to relate these two observations receives very strong support from the fact that some patients with gastro-enteritis of this type have very definitely shown evidence of increased lead absorption. While this has not been a constant finding it has been a very definite one as shown by the evidence of three different diagnostic methods (punctate basophilia, increased urine coproporphyrin and increased blood lead). The most conclusive of these methods - blood lead estimation - has been applied as will be shown later, to dogs as well as humans, and abnormal results have been obtained from three different laboratories.

On considering this evidence of increased lead absorption in association with some cases of gastro-enteritis, it must be recalled that in the specimen diet which was analysed, the lead content of the food was almost three times as great as that of the water. While noting that the lead content of the water can fluctuate within wide limits, if absorption of lead is to be linked with this type of gastro enteritis, then the lead content of foodstuffs must bear its full share of the responsibility. It is probable that the absorption of lead from food and certainly from milk, is much less than that from water taken on an empty stomach, but the estimations from patients represent the results of the total absorption from all sources.

The clinical features described, however, seem more in the nature of a local gastro-intestinal irritation affecting a number of persons simultaneously rather than the effects of a chronic poisoning. If a combined astringent effect was involved from lead, iron and copper derived from different sections of water piping, then wide variations in the amount of lead absorbed would be expected, and there might also be a considerable loss of the irritant material in the vomit and the diarrhoea.

Other possible causes of this gastro-intestinal disturbance must be considered. With poorly filtered or unfiltered water supplies and no chlorination, heavy rain could wash down bacteria from the catchment area. Bacteriological water sampling is regularly carried out and special samples taken at times of epidemics have proved quite unrewarding in this respect. Also a bacterial gastro-enteritis would have been expected to produce more positive results on culture of stools. For these reasons, no attempt is being made to dispute the claims of the Public Health

Authorities that these water supplies are satisfactory from a bacteriological point of view.

The offensive-looking, brown sediment in the water might in itself be a cause of gastro-intestinal disturbance. A standard book of reference on the subject (Thresh, et.al., 1958) gives assurance that there is no evidence that organic matter in water supplies is harmful.

Confirmation that lead in a particular form and in a particular quantity could cause gastro-enteritis would be more simply studied in a laboratory than in general practice. This is a very difficult subject, for a field study, as the number of possible variable factors is enormous.

The conclusion on this subject must therefore be that an association has been demonstrated between increased lead absorption and some cases of gastro-intestinal disturbance and that no other cause has been discovered for this condition. The source of the lead is the food and drink of the patient, and since the water provides an appreciable part of the lead intake, there are no grounds for disbelieving that an association exists between the gastro-enteritis and the water supplies.

Observation on Dogs.

It was noted that on some occasions, dogs were affected by diarrhoea and vomiting at the same time as their owners. Stool samples from two dogs were sent to a medical laboratory for bacteriological culture - with negative results.

Two dogs had full examination at the Royal (Dick) Veterinary College, including Blood Urea, Blood Count, differential White Cell Count, and Stool Culture, all with negative results. Blood Lead estimation was also done. Two other dogs were examined but had laboratory investigation limited to Blood Lead estimation only. One had had stool culture in a previous attack.

TABLE 31.

Blood Lead Levels in Dogs with Diarrhoea.

Dog 1. -	100 µg/100 ml.)	House L.
" 2. -	70 µg/100 ml.)	
" 3. -	115 µg/100 ml.	House M.
" 4. -	100 µg/100 ml.	House E.

Blood lead estimations on the last dog before and after the attack were 50 µg/100 ml. and 56 µg/100 ml. The normal blood lead level of animals is 0-25 µg/100 ml. (Garner 1961).

Distribution of Lead in Tissues of Dogs.

The owners were unwilling to allow further blood samples from Dog 3. When blood lead estimations were to be repeated on Dogs 1 and 2, it was found that Dog 2 was ill. The other dog, though not showing obvious illness at that time, had a very high blood lead level and developed a similar illness very soon afterwards. Both dogs had ataxia, inco-ordination of hind legs, anorexia, vomiting and faecal incontinence.

They were both over eleven years old and the owner confirmed that there was no question of the dogs being poisoned by licking lead paint or unusual exposure to petrol fumes. The dogs were destroyed but no significant Pathological lesion was found in either dog at post mortem (Royal (Dick) Veterinary College). Blood and tissue analyses for lead were done.

Since a full range of normal tissue levels for dogs is not available, the human figures given by Kehoe (1961) are listed for comparison. Goldblatt and Goldblatt (1956) found no accumulation of lead in the brain of animals inhaling inorganic lead compounds. With volatile organic lead compounds they suggested 0.2-0.3 mgm./100 G. in the brain as the critical level at which signs of encephalopathy might appear from inhalation experiments.

TABLE 32.

Dogs 1 and 2 - Tissue Analyses

Analyses done by the Royal (Dick) Veterinary College, Edinburgh.

Tissue Results are in Mgm./100 G. Blood Results are in µg./100 ml.

	DOG 1.	DOG 2.	Goldblatt Encephalopathy	Kehoe - Human Range	Normal Mean
Previous blood lead:	360µg.	70 µg.			
Blood lead at death:	150µg.	75 µg.			
Liver	2.47	0.42		0.04-0.28	0.12
Kidney	0.97	0.27		0.015-0.16	0.05
Brain	0.26	0.41	0.2-0.3mgm/100 G.	0.01 -0.09	0.04
Femur	0.27	0.10		0.67 -3.59	1.78
Rib		0.19		0.21 -1.11	0.65
Skull	0.24				

Results of four water analyses from that house ("L") in p.p.m.

0.99, 0.74, 0.20, 0.10.

The veterinary laboratory has attempted to confirm the significance of the brain lead figures of 0.41 and

0.26 mgm./100 G. by analysing a further twelve brains from dogs from various parts of the City of Edinburgh which were sent to the College for destruction. The results are given for comparison.

TABLE 33

The Lead Content of the Brains of Twelve Dogs.

Maximum:	0.11 mg./100 G.	fresh tissue.
Minimum:	0.02 mg./100 G.	do.
Mean:	0.05 mg./100 G.	do.

The distribution of lead in the tissues of these two dogs (1 and 2) resembles that found in poisoning with volatile organic lead compounds which are stated by Browning (1961) to have a specific affinity for lipoid and nervous tissue, unlike inorganic lead compounds which are much less toxic and are laid down in bone.

Dog 4, in addition to recurrent attacks of diarrhoea, developed weakness of the hind legs which prevented the dog jumping up into the owner's van - a height of 21 inches. This had been attributed by the owners to "Rheumatism". Calvery (1938) describes weakness of the hind legs as an early feature of lead poisoning in dogs. These symptoms disappeared with the installation of a polythene piped water supply at house E - (Previous maximum lead content 0.36 p.p.m.), though there was one recurrence of diarrhoea when the dog began drinking regularly from water dripping from an outside tap still connected to the lead supply. Two years after this recovery, the dog developed an intestinal obstruction from an acute inflammatory lesion of the small intestine which was considered at post mortem at the Royal (Dick) Veterinary College to have been produced by a foreign body in the gut.

The tissue analyses in this case show the heavy deposition of lead in the bone which is to be expected from previous chronic inorganic lead poisoning. The lead in the brain is more than in any of the Edinburgh dogs, but is below the level which Goldblatt associates with encephalopathy. The blood lead level is remarkable and must represent gross mobilisation of the large lead deposits in the bones produced by the cachectic state of the dog in its terminal stages.

DOG 4. - Tissue Analyses

	Lead in Mgs. per 100 gms.
Rib (dry, fat free)	7.1.
Femur (dry, fat free)	6.8
Liver (fresh)	0.135
Blood (whole)	1.28
Kidney (fresh	0.013
Brain (fresh)	0.149

Discussion.

While the analyses from Dog 4 are interesting in showing the magnitude of lead mobilisation which is possible, Dogs 1 and 2 provide a very difficult and serious problem. The distribution of lead in their tissues is like that of organic lead poisoning from tetra-ethyl lead. The owner is a particularly reliable witness and is very definite that there was no question of poisoning from petrol. It has been shown in the section on water supplies (page 78) that organic lead compounds occur in water, but that some of these are easily broken down by hydrochloric acid. It is difficult to imagine how an ingested organic lead compound could escape destruction by the processes of digestion, unless perhaps with an associated achlorhydria. Some organic lead compounds are much more toxic than inorganic lead salts. In view of this, laboratory studies seem very necessary to discover whether absorption of organic lead compounds as such, can take place from the gastro-

intestinal tract. If this should prove to be the case, then the accepted international standards for permissible lead content of drinking water might need to be revised to take into account the nature of the lead compounds involved.

Studies of Maternity Patients.

Blood lead levels in pregnancy.

Toward the end of these studies, facilities were provided for a small number of blood lead estimations to be done at the Laboratory of the Gardiner Institute at the University Department of Medicine, Western Infirmary, Glasgow (Lab.G). This laboratory is carrying out a programme of research on lead effects and has published information on the accuracy of their lead determinations (Goldberg, Smith and Lochhead 1963). This shows a standard deviation of ± 0.95 µg./100 ml. on a series of six samples of the same blood and ± 1.1 µg./100 ml. on a series of four samples of the same blood. The normal range for this laboratory for blood lead estimation is 22.9 ± 8.2 µg./100 G., (i.e., 14.7 to 31.1 µg./100 G.)

Blood samples (20 c.c.) were sent to this laboratory from nine maternity patients. The patients were selected in two instances because of known bad water supplies and one because of her raised urine coproporphyrin results and anaemia (9.1 gm./100 ml.). A well-controlled diabetic, not on insulin, whose baby died after six hours and an antepartum haemorrhage case were also included. The remaining patients were abortions occurring consecutively in the practice and an attempt was made in these to match the blood lead results with analyses of placental tissue and see if any relationship could be demonstrated. One of these abortion cases has been excluded from the table which follows because there has been confusion either in the laboratory labelling or in the results. This will be discussed later. Fuller details will also be given concerning those patients identified by numbers as well as initials.

TABLE 34

Blood Lead Levels in Pregnancy (Lab.G.)

Initials	Blood Lead µg./100 G.	Stage in Pregnancy (Weeks)	Notes
J.C. (Case Mat.1)	0.35	38	Premature Labour. (Farm B - very aggressive water)
S.P. (Case Mat.10)	24.6	39	Raised urine coproporphyrin. Anaemia.
B.R.	11.34	10	Abortion.
J.C.	9.4	11	Abortion.
E.J. (Case Mat.11)	3.16	12	Water supply containing 1 p.p.m. lead.
A.B.	0	1 week after Delivery	Perinatal death after 6 hours. Diabetic.
N.G.	0	11	Abortion.
M.E.	20.37	32	Antepartum haemorrhage.

It is obvious that the majority of these figures are well below the lower limit of normal from the laboratory. They are so very low that if they had been provided by a laboratory inexperienced in this analysis they would immediately have been doubted. A similar very low figure 2.38 µg./100 ml. had previously been reported by another laboratory (Lab.P.) in case Mat.1 (J.C.). It is necessary to give some consideration to the factors of pregnancy which might interfere with blood lead levels and with their interpretation.

According to Baird (1962), the plasma volume rises in pregnancy by almost 50% at thirty weeks and thereafter there is little change until term. The red cell mass rises by only 20% and therefore there is an obvious dilution of red cells - the so-called physiological anaemia of pregnancy. This is at a maximum at about the thirtieth week.

Dieckmann and Wegner (1934) state that the increase in plasma volume begins in the first trimester and by the thirteenth week it is of the order of 18 per cent. It is generally accepted that 90 per cent. of the lead in the blood is contained in the red cells. Stewart and Stolman (1960) provide no less than eight references confirming this point. The dilution of red cells occurring in pregnancy, therefore, will obviously cause a lowering of blood lead figures. While this will be of great importance in considering the level which may be regarded as toxic, it could not be expected to produce the very low figures in Table 34.

It is known that decalcifying conditions cause mobilisation of lead from the bone and an increased blood lead level (Brown, 1946).

A well recognised method of increasing the elimination of lead is the production of a chemically induced acidosis by the administration of ammonium chloride (Hunter, 1957).

The converse of these observations is also true. Lead is stored in the bones in conditions favourable to a deposition of calcium (Stewart and Stolman 1960). Irving (1957) describes a positive calcium balance as being maintained in pregnancy. At the end of gestation the mother has stored far more calcium than is needed, but this extra storage may be due to previous deficiencies in the calcium intake. In contrast, in lactation in animals and humans, there is a negative calcium balance with mobilisation from bone for milk formation.

Dieckmann and Wegner (1934) record that the carbon dioxide of the blood is decreased from 6 to 10 per cent. by volume during pregnancy and the total base is decreased, reaching a minimum at term of 4 to 6 millimols below normal. There is, therefore,

in pregnancy a condition of compensated alkalosis or carbon dioxide deficit.

These alterations in the blood chemistry in pregnancy must be responsible for the very low blood lead levels just quoted. They give no grounds, however, for concluding that the unbound lead in the serum is correspondingly lowered. If this were the case, then pregnancy would be expected to have a protective influence with regard to lead poisoning, but this is at direct variance with clinical experience in this subject.

The patient who was excluded from the above series also had an abortion (at nine weeks). A sample (20 c.c.) of blood was forwarded to the laboratory in two heparinized containers. A specimen of placental tissue was sent to the same laboratory for lead estimation two days later. The laboratory reported two separate figures for blood lead estimation - 43.36 and 25.34 µg./100 G., but subsequently stated that they were unable to trace the placental tissue. The two blood samples were taken from the same syringe and were forwarded in separate containers because of doubts about the quantity of anticoagulant in the bottles. It is not now clear whether this is a laboratory fault giving different results for two separate samples of the same blood, or as seems much more likely, whether one of these two results refers to the placental tissue, which was analysed at the same time as the blood samples but has been inadequately labelled in the laboratory. If that is the case, then there is no way now of knowing which result refers to blood and which to placenta.

A sample of placental tissue in respect of patient B.R. was reported as having a lead content of 4.42 µg./100 G. A sample of placental tissue sent from the abortion case, J.C., was initially reported as containing 74.56 µg./100 G. This seemed a high result and was, therefore, repeated, but the repeat

sample was reported as containing 0 µg./100 G. The explanation for this large difference was that only 3 to 4 G. samples of placenta were used and when these were multiplied up to 100 G. quantities, the differences were magnified considerably. The actual figures involved in the calculations were:

First Sample - 4.0236 G:- Lead estimated 0.0365, Blank 0.0025.
Second Sample - 3.5341 G:- Lead estimated 0.0230, Blank 0.0250.

It is very difficult to draw any conclusions from figures of this sort.

With the remaining abortion (N.G.) a request was made to the Registrar of the unit concerned at the time of her admission for the retention of placental tissue for analysis. The reason for the request was explained. Despite this, the products of conception were inadvertently discarded after the uterus had been evacuated.

Attempts at comparison of the lead content of blood and placental tissue in these four cases were, therefore, completely unsuccessful, as unequivocal results were obtained for both blood and placenta in only one case.

The request for relatively large (20 c.c.) blood samples for lead estimation by the laboratories can be better appreciated in view of the figures just given for the placenta of J.C. Large samples reduce distortion of the results in the multiplication required to quote the figures as - per 100 G.

Reference has already been made in the historical section to the increased susceptibility of the woman and especially the pregnant woman to the effects of lead.

While these studies were commenced in the first instance because of interest in a gastro-enteritis, attention was soon focused on the maternity patients

after the discovery of the plumbo-solvent tendencies of the water supplies. A patient with a very bad water supply had a miscarriage when seven weeks pregnant in association with diarrhoea and also with a raised punctate basophil count.

Case No. Mat. 1. Mrs. J.C., Age 32.

This patient's water supply (Farm B.) has already been described in detail. It was extremely unsatisfactory showing a great deal of sediment after heavy rainfall and the maximum lead content from water samples from this farm was 0.90 p.p.m.

Previous Obstetric History:

13/7/53 - Antepartum haemorrhage at 6½ months followed by premature birth. Baby died after a few hours.

14/11/54 - Miscarriage at 9 weeks.

19/8/56 - Forceps Delivery at term. Baby normal.

17/4/59 - Antepartum haemorrhage at 32 weeks. Spontaneous Delivery at term. Baby normal.

5/7/60 - Miscarriage at 7 weeks.

14/11/60 - Miscarriage at 7 weeks associated with diarrhoea. Punctate basophil count 0.5%, Hb. 13 g./100 ml.

The history, therefore, was of two surviving children out of six pregnancies, the last pregnancy having ended in a miscarriage with a raised punctate basophil count.

By the time of her next pregnancy, facilities for blood lead estimation were available.

19/4/61 - Threatened miscarriage at 7 weeks. Hb 12.6 g./100 ml. Punctate basophils 0.25%. Blood lead 53 µg./100 ml. (Lab. P.)

This pregnancy continued and at twenty weeks, since the patient was complaining of vague abdominal pain in right and left iliac fossae, these tests were repeated. In the meantime, the patient had had

treatment with calcium gluconate and the temporary provision of a water supply with a much reduced lead content.

22/7/61 - Hb. 12.3 g./100 ml. No punctate basophils seen. Blood lead 2.38 µg./100 ml. (Lab.P.)

Urine coproporphyrin estimations at the 35th and 36th weeks of pregnancy gave results Donath scale 2 (50-100 µg./litre). At 36 weeks of pregnancy this patient had an antepartum haemorrhage followed by a premature delivery of a 5 lb. 2 oz. child.

This patient again became pregnant in 1963 and again had a threatened miscarriage at her 11th week.

Urine Coproporphyrin Results in Pregnancy (Donath Apparatus)

Weeks of Pregnancy	Before 28	29-32	33-36	37-38
Results on Donath Scale	2,1,1,1	2	2,3	4,3

At 38 weeks, she had a premature labour with spontaneous delivery of a normal 6 lb. baby. At this time, her blood showed no punctate basophilia, Hb 12.3 g./100 ml. Blood lead 0.35 µg./100 g. (Lab.G.)

This patient showed a very definite pattern of miscarriage or threatened miscarriage in early pregnancy and if the pregnancy continued, either antepartum haemorrhage or premature labour. With each of these antepartum haemorrhages she had full hospital investigation and placenta praevia was excluded.

With a bad water supply such as this one, a miscarriage in association with a punctate basophil count of 0.5% must be presumed to be due to lead. A threatened miscarriage with a punctate basophil count of 0.25% is suspicious and the blood lead level is certainly higher than any of those in Table 34, but the stage in pregnancy is also earlier. In the last pregnancy, the urine coproporphyrin excretion rose to a level which I have only recorded in one other maternity

patient in this practice. Despite this distinctly unusual reading and the progressive rise which preceded it, there was no punctate basophilia and the blood lead level was extraordinarily low. This urine coproporphyrin result can only be regarded as suspicious and not conclusive. While raised coproporphyrin can precede punctate basophilia (de Langen and ten Berg 1948) and rise in urine lead level (Zielhuis 1961) this test is not specific for lead. It cannot, therefore, be claimed that the premature labour was due to the effect of lead, but only that it was associated with a suspicious rise in urine coproporphyrin level.

The landlord has now given his co-operation in the improvement of the water supply of this farm.

Case No. Mat.2., Mrs. E.R., Age 22, Para 1.

On 15/3/61, this patient attended when twelve weeks pregnant, complaining of diarrhoea for two weeks and vomiting intermittently for eight weeks. The diarrhoea occurred especially after breakfast which consisted of a cup of tea and a roll. The vomiting was never morning sickness, always occurring in the afternoon and evening. She also complained of a bad taste in the mouth which she described as being like "the sucking of an acid drop". She was listless and lethargic and had recurring spasms of pain in right and left iliac fossae. On examination, she was found to have tenderness over her caecum and over her descending colon. The size of her uterine enlargement agreed with her expected date of delivery, but her uterus was very markedly tender. Bacteriological culture of stool - no intestinal pathogens isolated. Haematology - Hb. 10.5 g./100 ml., P.C.V. 35, R.B.C. 3.99 million M.C.H.C. 30%, M.C.V. 87, E.S.R. 8 mm. in 1 hour (West.), W.B.C. 4,500 /cu.mm. Punctate basophil count - stippled cells present but less than 0.1%, very scanty.

Blood lead estimation - 31 µg./100 ml, urine lead estimation - 119.7 µg./24 hours (90 µg./litre) (Lab.P.) This patient was treated with Avomine (Promethazine Theoclate), Ostocalcium (calcium and vitamin D), Chalk and Opium mixture (B.P.C.) and Fersamal (Ferrous Fumarate). The diarrhoea and vomiting continued for the next three days, but by the fourth day the patient felt very well indeed and volunteered the information that she had that day spring cleaned her whole house and done a big washing. A second urine lead estimation ten days after the first, showed a marked fall in lead content - 38 µg/24 hours (30 µg./litre).

She had no further gastro-intestinal disturbance until 28/8/61 (36 weeks pregnant) when she reported that she had had diarrhoea for two weeks, four to five times per day. Her appetite remained good, she had no vomiting, but was troubled by flatulence and eructations. She had no abdominal pain, but a discomfort in both right and left sides of her abdomen. This patient was greatly troubled with chilblains each winter and she commented that her chilblains seemed to be restarting already though it was only the end of August. Blood film examined at that time and five days later showed no punctate basophilia. Blood lead estimation, however, was reported as showing 237 µg./100 ml. (Lab. P.). The urine showed a trace of albumin and this was still present the following week, but there was no oedema.

At the 39th week of pregnancy a sudden increase in weight of 7 lbs. in a week was recorded. There was a trace of oedema, no albuminuria, and the blood pressure was 120/60. On the next day the patient had an accidental haemorrhage (continuous lower abdominal pain for two hours, followed by frank bleeding). She then started in labour and was delivered spontaneously of a 6lb. 3 oz. baby after twenty hours. The baby was

normal except for a haemangioma on the wrist. A blood film examined ten days after delivery showed no punctate basophilia.

The haemangioma increased in area till it was a raised red plaque about the size of a penny. Then its colour progressively faded from the centre outwards and by the age of three, only a faint residual staining and skin roughness remained.

Water Analyses - A single water sample examined at the time of the first attack of diarrhoea in March 1961 showed a pH of 7.2, lead content Nil. Two samples examined on 28th and 29th August 1961 had pH 7.1, lead content 0.17, and pH 7.2, lead content 0.16. A further sample on 14/3/62 had pH 6.7, lead content Nil.

Supervision of Maternity Patients by Urine Coproporphyrin Estimation.

As a result of the experience with these two cases in 1961, it was felt that there was a need for some method of supervision of maternity cases similar to that adopted in lead-using industries for supervision of workers. This seemed necessary until the water supplies were improved to eliminate the plumbo-solvent tendencies. Regular urine coproporphyrin estimation by the Donath apparatus was adopted as likely to show the earliest signs of lead toxicity. This was supplemented by punctate basophil counts and blood lead estimations. As has already been mentioned in the section on laboratory methods (p. 56), the original levels described by Donath (1956) as normal were reconsidered because of further observations by Zielhuis (1961). The results obtained from using this apparatus for a year and from supplementary tests were such that it was necessary to make attempts to limit the lead intake of the maternity patients in the practice.

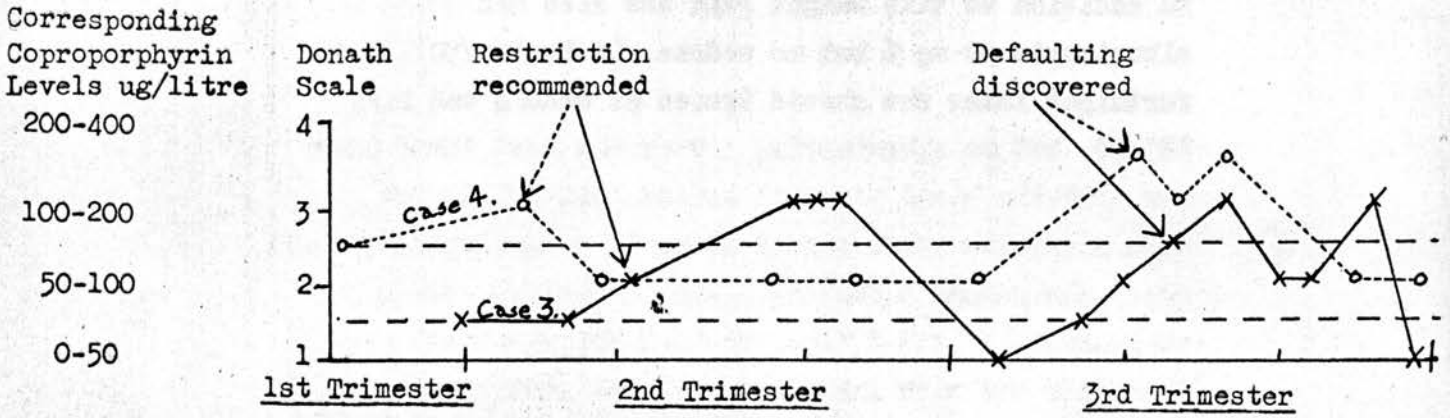
It was felt that it would be most undesirable to create a local panic among maternity patients by drawing attention to the fact that they were absorbing lead from their water supplies. Their attention was, therefore, directed to the need for increasing their intake of milk and therefore of calcium for the benefit of the baby. They were also warned that excessive fluid intake was sometimes associated with oedema later in pregnancy. While drinking more milk, therefore, they should attempt to restrict water and tea to one pint per day and have the remainder of their fluid intake as milk, either alone or as coffee or cocoa.

This simple measure was followed by a difference in the pattern of urine coproporphyrin results and after some little time it was appreciated that this gave an opportunity for a comparison between two groups of patients. The maternity patients attending during a two year period and all their routine ante-natal urine samples were made the subject of a special study. It was possible to divide these patients into two separate groups, one of which had been subject to no water restriction and the other which had water restricted and milk intake increased. All routine urine samples from all the maternity patients were used from October 1961 to September 1963, with the exception of two cases which will be described. It is not possible to be certain how many of the patients observed the recommendation that they should restrict their water intake. Most, when asked, said that they were doing so. Two patients, however, were definitely known to default.

<u>Defaulters from water restriction regime.</u>

Before considering any group of results the details of these two cases will be given. These patients were asked to restrict their water intake but on questioning subsequently said they had not done this.

Fig. 8. Fluctuations in Urine Coproporphyrin Excretion during pregnancy in two patients who did not maintain restriction of water intake.



The transverse lines are the levels associated by Zelhuis (1961) with industrial exposure (1.5) and exposure exceeding permissible limits (2.5) with group results

Facing page 169.

The results of the routine coproporphyrin tests on urine samples brought throughout pregnancy can be shown as a graph (Fig. 8).

Case No. Mat.3., Mrs.J.P., Age 19, Primipara.

This patient was asked if she was maintaining her water restriction at 34 weeks when it was noted that she had suddenly gained 11 lbs. in weight in a fortnight. She readily admitted that she had not been doing so. In addition to this weight gain she also had albuminuria 30 mg.% but no oedema, (B.P. 125/50). A fortnight later she showed traces of oedema and B.P. 135/80, but no albuminuria. Over the next three weeks her systolic blood pressure ranged from 130 to 140 with diastolic pressures of 70 or 80 and on one occasion 90. She gained a further 2 lbs. in weight and then progressively lost 6 lbs., without any treatment or diuretics but with increased rest and reduced salt intake. Four days after her expected date of delivery, labour was induced in the Western General Hospital, Edinburgh, by artificial rupture of membranes and a normal 7 lb.15 oz. baby was delivered spontaneously.

It should be noted that the rise in urine coproporphyrin level in this case following water restriction does not necessarily mean that the patient was defaulting at that time. De Langen and ten Berg (1948) described periods of five to eight weeks for clearing of abnormal coproporphyrinuria after the stopping of experimental lead exposure in human subjects. If such a time lag applied in Fig. 8 , the fall in coproporphyrin excretion recorded at the beginning of the third trimester could have been a consequence of the restriction in water intake recommended in the second trimester. This time lag in the appearance and clearing of excess urine coproporphyrin is of more importance in this study of maternity patients than in studies of

industrial cases. Because of this time lag the coproporphyrin test is demonstrating effects of a toxic process which occurs some days or even weeks previously.

Further information concerning this case - The baby developed a marked infantile eczema at two months and this persisted for six months. A Consultant Paediatrician who saw the child at four months, because of this commented that there did not appear to be a strong allergic history in this family.

Mrs. J.P. aborted at the ninth week in her second pregnancy. Hb. 14.3,g./100 ml., punctate basophilia - very occasional stippled cells present, less than 0.1%. The confusion over her blood lead estimation has already been mentioned (p.161). After 24 hours observation as a threatened miscarriage, she was admitted to hospital as an incomplete abortion and evacuation of the uterus was carried out. Urine coproporphyrin - 2½ degrees on the Donath scale.

Case No. Mat.4, Mrs. I.D., Age 19, Primipara.

This patient had a urine coproporphyrin of 3 degrees on the Donath scale when twelve weeks pregnant, at the time when she was requested to limit her intake of water. The level of the Donath readings fell to 2, but rose again to 3½ at 33 weeks pregnancy. She was asked at her next attendance about the amount of water she drank and said that she did not like milk. Her fluid intake was estimated at 3½ pints of water and 2/3rd of a pint of milk, mostly made into puddings. She was again asked to restrict her total intake of water to one pint and her total fluid intake to 2½ or 3 pints per day, comprising milk, water and lemonade, but at this time she showed a trace of albumin in the urine, B.P. 120/80, and no oedema. During the remainder of her pregnancy her blood pressure progressively rose till at her

expected date it was 140/100. Nine days before she was due she had a trace of oedema and though this was treated with Bendrofluazide (Neo-Naclex), rest and Amylobarbitone, the oedema persisted. She was admitted to Peebles War Memorial Hospital for medical induction at term and had a spontaneous delivery of a 8 lb.1 oz. baby, but this was followed by a post partum haemorrhage of 40 ozs. The baby was normal at birth but subsequently developed a large haemangioma on the left thigh.

Because of the difficulty of allocating these two patients to groups subject to water restriction or unrestricted, they have been excluded from the series which follows.

Comparative series.

Though water restriction for maternity patients was introduced as a temporary prophylactic measure until the water supplies were improved, it was subsequently realised that this provided an opportunity for a comparison. The total number of pregnancies for which ante-natal care was provided during a two-year period was 75 (72 patients), excluding the two defaulters mentioned above. They were divided into those subject to no water restriction, and those having a variable duration of water restriction during pregnancy, depending on the time in the second year when they attended. Age and parity comparisons for the two groups are given in Table 35.

TABLE 35

Age and Parity Comparison of Two Groups of Pregnancies

	No Water Restriction Group A	Water Restriction Group B
Age - over 28 at first attendance	13	12
between 21 and 28 at first attendance	16	21
20 and under at first attendance	6	7
Primipara	12	18
Para 1, 2 and 3	19	19
Para 4 and over	4	3
	35	40

To obtain a normal control series from non-pregnant women all patients in the practice who had attended for ante-natal care between October 1961 and September 1963 were asked to supply two urine samples at intervals of a week during February and March 1964. Those patients who were again pregnant or were lactating were excluded from this series and there had been a certain number of removals from the area. There were forty-five patients remaining from the original pregnancy series and all these supplied urine samples taken at the same time of day as the samples they brought during pregnancy.

The Results.

The results are given in Table 36 according to the highest reading for each patient from a number of urine tests with the Donath apparatus. There is a distinct difference taken over the whole of pregnancy between the two groups.

TABLE 36

Comparison of Effects of Water Restriction on Urine Coproporphyrin Excretion in Pregnancy

	Maximum Donath Reading	Corresponding range in ug./litre	Whole Pregnancy Group A Unrestricted Patients	Whole Pregnancy Group B Restricted Patients	Non-pregnant Controls. Groups A & B Unrestricted
No. of Patients reaching each level.	1	0-50	10	26	30
	2	50-100	14	13	14
	3	100-200	10	1	1
	4	200-400	1	-	-
			35	40	45

For making a test of reliability of comparison between restricted and unrestricted patients, it has been assumed that these two groups are in all other aspects similar. It will be shown that season of year seems to influence the results but in this comparison both groups were studied through all seasons.

For test of significance the three patients having two pregnancies were excluded from both groups so as to permit the use of the patient for the unit of analysis without bias. This excludes one Donath reading 1, one Donath reading 2, and two Donath reading 3 in Group A, and one Donath reading 1, and one Donath reading 2 in Group B.

The difference between groups A and B in their Donath distribution is statistically significant at $P < .005$.

TABLE 37

Comparison of Effects by Trimesters

			1st Trimester			2nd Trimester			3rd Trimester		
			A	B	B	A	B	B	A	B	B
	Maximum Donath Reading	Corresponding range in ug/litre	Unrestricted throughout	Restricted throughout	Unrestricted then Restricted	Unrestricted throughout	Restricted throughout	Unrestricted then Restricted	Unrestricted throughout	Restricted throughout	Unrestricted then Restricted
No. of Patients reaching each level.	1	0-50	4	No Samples	2	10	10	13	6	19	2
	2	50-100	1		1	12	3	3	13	7	3
	3	100-200				1	-	-	10	-	1
	4	200-400				-	-	-	1	-	-

Clinical Features of Comparative Series of Maternity Patients.

With an interference in the water intake of maternity patients and an alteration to their diet by increasing their consumption of milk, and therefore of calcium, it was necessary to see whether any other effects had been recorded in either group of patients, apart from the difference in urine coproporphyrin excretion which has already been described.

The number of patients showing glycosuria at some time during pregnancy seemed very high, but when the two groups were compared there was little difference. Clinistix and Albustix tests make use of enzyme reactions and lead interferes with certain enzymes (Goldblatt and Goldblatt 1956). The manufacturers - Miles Laboratories Ltd. (Munro 1962) state that these tests are unaffected by 0.2 mg./litre of lead in the urine specimen. The large proportion of positive Clinistix results (over 50 per cent.) is likely to be related to the fact that the test was read at exactly one minute as recommended by the makers and recorded as positive if any blue colouration

was seen. I had previously been less precise in timing this test and had recorded positive results much less frequently. Sugar-free specimen bottles were provided to eliminate contamination. The maternal weight gains had been recorded from the date of first attendance, but there was some variation in this date between the different pregnancies. Both maternal and baby birth weights are incomplete because certain patients moved into or out of the practice during the course of their pregnancies.

Since the suggestion had been made (Porritt 1934) that there was an association between eclampsia and plumbo-solvent water supplies, the features associated with pre-eclamptic toxaemia were extracted for all the pregnancies studied and are presented as a subsidiary table. These features have only been listed if they occurred after the 24th week of pregnancy. Elevations in blood pressure early in pregnancy have not been included. Since primiparity is a major aetiological feature in pre-eclamptic toxaemia it should be recalled that the water restriction Group B had a slightly increased proportion of such patients (eighteen out of forty) compared with Group A with no water restriction (twelve out of thirty-five).

TABLE 38

Clinical Features of Two-Year Series

	No Water Restriction Group A	Water Restriction Group B
Total Numbers in each group	35	40
Glycosuria - Positive Clinistix	18	22
Positive Clinitest ¼% or more	10	10
Maternal Weight Gain of less than 20 lb.	16	18
" " " between 20 - - and 30 lb.	15	16
" " " of more than 30 lb.	-	3
Birth Weight below 6½ lb.	4	6
" " between 6½ and 7½ lb.	11	19
" " above 7½ lb.	17	12
Premature labour before 38 weeks	3	2
Stillbirth	1	1

TABLE 39

Features of Pre-eclamptic Toxaemia

	Group A	Group B
Systolic B.P. of 140 or above	19	11
" " " 130 " "	25	22
Diastolic B.P. of 90 or above	16	10
Albuminuria	21	8
Oedema	15	11

In none of the features of Pre-eclamptic Toxaemia does the water restricted group reach equality in number with the unrestricted group, in spite of the slightly larger size of the group. The comparison becomes more striking when the patients showing two or more symptoms are extracted for each group. Sixteen patients had a systolic B.P. of 140 or above plus Albuminuria. Fifteen

of these were in the unrestricted group and only one in the restricted group. Of fourteen patients with hypertension of this order and oedema, ten were unrestricted and four restricted. Only six patients showed all the features: Systolic B.P. of 140, Diastolic of 90, Albuminuria and Oedema. All these six patients were in the group which had been subject to no water restriction.

These numbers are small and the observations were not made originally with a view to obtaining comparative information on Pre-eclamptic Toxaemia. A large carefully controlled study would be necessary before a definite conclusion could be reached. They do, however, provide clinical observations on Porritt's (1934) Thesis that Eclampsia was related to plumbo-solvent water supplies. Such evidence as can be provided by groups of this size suggests that reduction in intake of water and increase in milk consumption has been associated with a lessening in the frequency of occurrence of these features of Pre-Eclamptic Toxaemia. Whether this effect is due to reduction in lead absorption, to increase in calcium absorption, or to reduction in total fluid intake is quite unknown. In view of the striking nature of some of these observations, further studies are indicated to see if these can be confirmed and if so, to discover how this effect has been produced.

Ante-natal Urine Samples from Other Areas.

A series of urine samples was obtained from the Simpson Memorial Maternity Pavilion Ante-natal Clinic and these were tested on the Donath apparatus. The samples were obtained from May to November 1962.

TABLE 40

Hospital Results - Ante-natal Cases

Donath Scale	1	-	361
	2	-	35
	3	-	5
	4	-	1
	5	-	2
Total:			404

Average (degrees Donath): 1.18.

From these results it will be seen that only 2 per cent. of the patients in this series reached or exceeded the Donath level of 3 (100-200 µg./litre). This must be compared with Zielhuis' (1961) figure of 10 per cent. of males in industry with no occupational lead exposure showing this level of urine coproporphyrin excretion. One of many possible reasons for this difference is the influence of alcohol on the results since the Dutch industrial workers might take alcohol more freely than the Edinburgh maternity patients. It was not possible to make a detailed study of these patients. They are not representative of normal pregnancy for many were booked for medical or obstetric abnormalities. It should also be recalled that some of Edinburgh's water supplies come under suspicion of plumbo-solvent tendencies because of their pH levels.

Of the two patients showing degree 5 on the Donath scale, one had an ante-partum haemorrhage and premature labour at 34 weeks, soon after her ante-natal urine sample was obtained. Her baby had no congenital abnormalities (weight 4 lbs. 10 ozs.), but she took her own discharge from hospital soon after delivery and there was no follow up. The other patient with this grossly abnormal degree of coproporphyrinuria had a spontaneous delivery of a normal 7 lbs. 5 oz. baby. Blood films were obtained from this patient, but no punctate basophilia was found. The only abnormalities

noted during pregnancy were a brown discharge at the thirteenth week and an excessive weight gain throughout pregnancy, totalling 62 lbs., for which she was treated with Saluric (Chlorothiazide). It seems probable that this patient and the patient giving the Donath reading 4 are both supplied from the softest of Edinburgh's three water supplies, but it has not been possible to make further investigations either of the patients or of their individual water supplies.

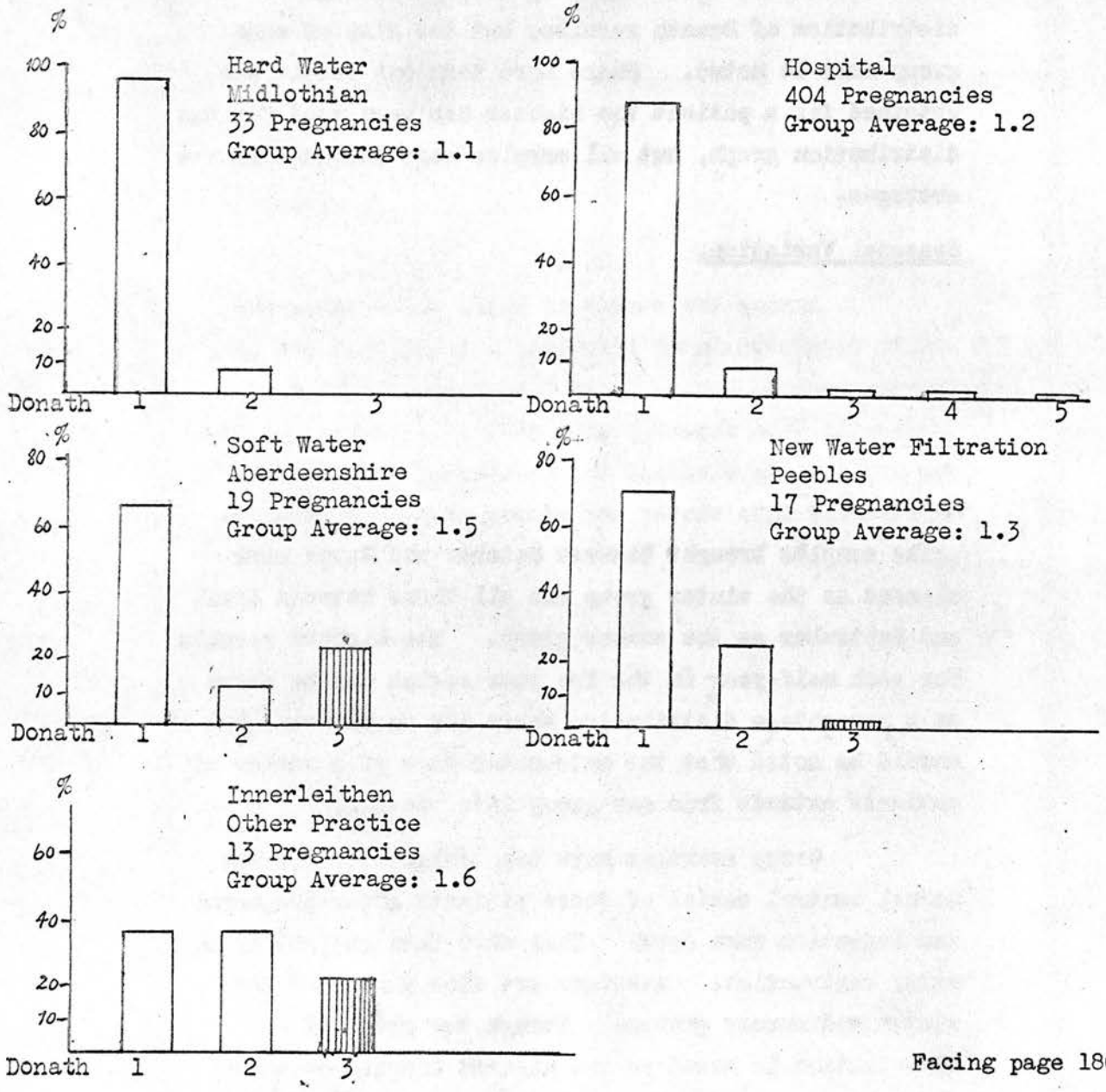
Other Areas.

A series of urine samples was obtained from the ante-natal patients of a Midlothian practice on a hard water supply. A total of fifty-seven samples was obtained from thirty-three patients. Only two patients out of this series showed urine coproporphyrin at the level of Donath scale 2, and both these at some other time had results in the Donath scale 1 range. These samples were obtained in April, May, June and September 1963. By contrast when the Donath apparatus was used by a practitioner in Aberdeenshire in August and September 1963, of nineteen patients who had urine samples tested, four showed urine coproporphyrin results in the range Donath scale 3, two at the Donath 2 level, and the remainder gave Donath readings of 1.

To the urine samples from these groups of maternity patients can be added a small series obtained from a doctor in Peebles. This town has very recently installed a large modern water treatment plant. Certain patients were seen in Innerleithen under deputising arrangements with my colleague in the town and have not been included in my two year study. Average results for the Donath readings of these groups have been calculated. According to Zielhuis a group average of 1.5 degrees on the Donath scale is associated with increased lead intake in industry. Certain of the

Figure 9.

Percentage distribution of Donath results in urine samples from groups of maternity patients.



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groups reach or exceed this average, but none approach the limits of permissible industrial exposure for male workers which Zielhuis gives as 2.5 degrees Donath. It is difficult to present these results in a form suitable for comparison. In Fig. 9 they have been shown for convenience according to a percentage distribution of Donath results, but the size of each group must be noted. Where more than one result was obtained for a patient the highest has been used for the distribution graph, but all samples were included in the averages.

Seasonal Variation.

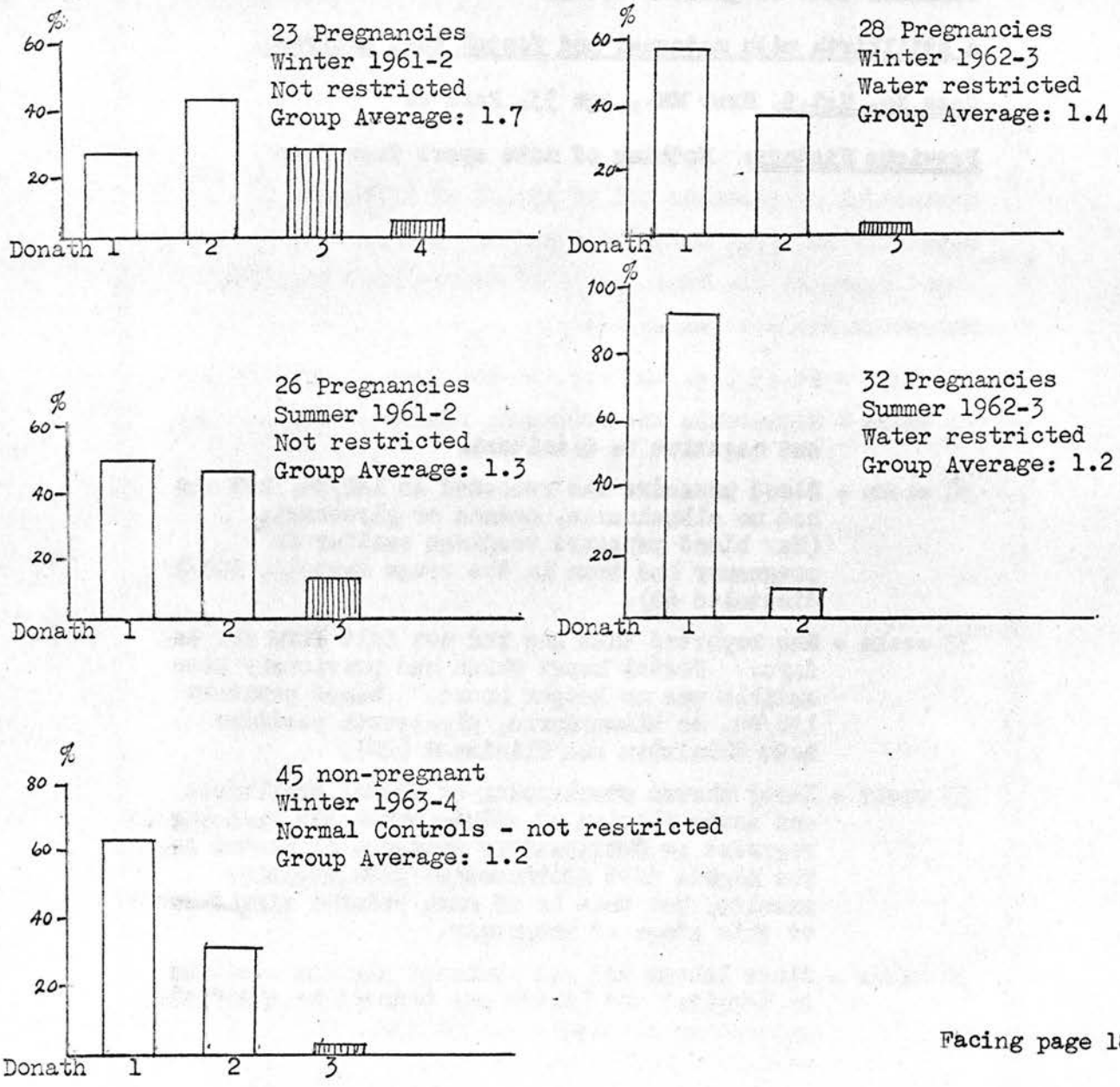
During the summer of 1962, while using the Donath apparatus in my practice, I noted that the pink fluorescence of Donath 3 was occurring much less frequently than formerly with maternity patients. This was explored by dividing the results of urine tests arbitrarily into winter and summer groups. All the urine samples brought between October and March were classed as the winter group and all those between April and September as the summer group. The highest results for each half-year in the two year series can be shown on a percentage distribution basis for comparison, but it should be noted that the ante-natal care of a number of patients extends from one group into another.

Group averages have been calculated for the normal control series of these patients after pregnancy and lactation were over. They were then subject to no water restriction. Averages are also shown for the winter and summer groups. Though the graph of distribution is based on the highest results obtained, the group averages are calculated on the basis of all samples brought during the two year period (totalling 713 estimations). See Fig. 10 .

This shows evidence of a variation in the results between summer and winter affecting both water

Figure 10.

Pregnancy Urine Samples;- Seasonal variation in maximum results with Donath apparatus.



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restricted and unrestricted groups. Variations between summer and winter in rainfall, in organic matter content of water supplies and in lead content, have already been described in previous sections.

Some of the maternity cases studied during these two years have noteworthy features which are not illustrated by group observations. It is, therefore, necessary to consider them in greater detail.

A stillbirth with maternal and foetal lead analyses.

Case No. Mat.5, Mrs. MM., Age 33, Para 4.

Previous History: Nothing of note apart from four uneventful pregnancies and an attack of infective hepatitis one year before the present pregnancy commenced. Blood Group A, Rh. Neg., Indirect Coombs Test negative, Wasserman and Kahn negative.

18 weeks - Hb.13.9 g./100 ml., no punctate basophilia seen.

26 weeks - Glycosuria was recorded, positive to Clinistix, but negative to Clinitest.

30 weeks - Blood pressure was recorded as 140/86, but she had no albuminuria, oedema or glycosuria. (Her blood pressure readings earlier in pregnancy had been in the range systolic 100/120, diastolic 60).

33 weeks - She reported that she had not felt life for two days. Foetal heart which had previously been audible was no longer heard. Blood pressure 130/80, no albuminuria, glycosuria positive both Clinistix and Clinitest (¼%).

35 weeks - X-ray showed overlapping of foetal skullbones and acute flexion of spine, which the radiologist regarded as confirmatory evidence of foetal death. The Hogben test continued to give positive results, but this is of much reduced significance at this stage of pregnancy.

36 weeks - Since labour did not commence she was admitted to hospital and labour was induced by artificial rupture of membranes and pitocin drip. A macerated foetus was delivered spontaneously.

Laboratory Investigations:

33 weeks - Indirect Coombs test negative, Haematological examination - no abnormality. Hb 14 g./100 ml., P.C.V. 42, M.C.H.C. 33, E.S.R. 18 mm/1 hr. W.B.C. 8,700/cu.mm. No stippled cells seen in blood film. Fasting blood sugar 48 mg./100 ml. Blood lead 55 µg./100 ml.

Husband's Blood Group O, Rh positive, Wasserman and Kahn negative.

34 weeks - Blood film, punctate basophilia present, less than 0.1%. Blood lead 34 µg./100 ml., Urine lead 86 µg./24 hrs. Carbon dioxide combining power 23 M.Eq./Litre.

35 weeks - Blood lead 72 µg./100 ml. Fasting blood sugar 76 mg./100 ml.

2 weeks after Delivery - Hb 12.7 g./100 ml. Blood film - no stippled cells seen.

2 months after Delivery - Blood lead 51 µg./100 ml.

Urine Coproporphyrin Results in Pregnancy (Donath apparatus)

Weeks of Pregnancy	Before 28,	29-32	33 - 36
Results on Donath Scale	1, 2	1	2, 2½, 2½, 2, 2½, 2½, 1½, 1

Post Mortem Examination of Foetus (Royal Hospital for Sick Children, Edinburgh.)

External Appearance: a severely macerated female foetus weighing 2190 g.

Head: Brain was semifluid as a result of maceration.

Thorax and Abdomen: the whole trunk was exceedingly pale.

Post mortem examination failed to reveal any developmental abnormality in thorax or abdomen. All the organs were extremely pale and bloodless. There was nothing to indicate haemolytic disease.

Summary: Exsanguinated foetus.
No evidence of haemolytic disease.
Maternal hyperplumbism.

Because of the macerated condition of the foetus no histological examination was possible from any organ.

Tissue Lead Analysis:

The Committee on Lead Poisoning of the Industrial Hygiene Section of the American Public Health Association (1943) published figures for comparative purposes with the following comment.

"The range of normal lead concentrations in the various tissues of the adult human being has not been established in an entirely comprehensive manner and therefore slight deviations should be interpreted with caution. Nevertheless, the following figures on the tissues of North Americans with no occupational or unusual lead exposure, may be used as the basis for comparison. The concentrations are given in milligrams of lead per 100 grams of fresh or formalin-fixed tissue."

This normal range is also quoted by Kehoe in the Harben Lectures to the Royal Institute of Public Health and Hygiene 1961, and so should not be considered to be out-dated.

Since suitable normal figures from foetal tissues are not available for comparison, these adult human results have been used for comparative purposes.

		Liver	Kidney
Adult Normals.	Mean	0.12 mg./100 gm.	0.05 mg./100 gm.
	Maximum	0.28 "	0.16 "
	Minimum	0.04 "	0.015 "

Samples were provided from liver, kidney and bone, but because of difficulty in ashing the bone sample the laboratory was only able to provide results for the liver and kidney samples (Lab.P).

Liver - 0.053 mg./100 gm.
Kidney - 0.200 mg./100 gm.

Water intake and water supply of this patient:

This patient had a very high maximum fluid intake estimated at 5.2/3rd pints of water and tea and usually drank 4½ pints every day. This was in addition to water used in cooking and about two-thirds of a pint of milk. She drank a cup of hot water soon after rising each morning for its laxative effect and quite often used the domestic hot water supply to fill her

kettle. Her council house was built in 1952. The internal water supply pipes were copper, but there was a length of lead pipe underground from the main on the other side of the street to the kitchen at the back of the house, a distance of 110 feet.

Water analysis:

Cold water (8 samples) Lead content average 0.055, range: trace to 0.11 p.p.m.
pH range 6.2 to 6.9.
Hot water system (2 samples) 0.109, 0.11 p.p.m.
Gas geyser in kitchen (1 sample) 0.16 p.p.m.

Discussion

At the time of intra-uterine death of the foetus, the possible causes appeared to be Haemolytic Disease, Diabetes or toxic effects of lead. The Indirect Coombs Test was negative and fasting blood sugar results were normal. The urine coproporphyrin test while showing a definite pink fluorescence was not greatly increased and there was, initially, neither anaemia nor punctate basophilia. It has been known for many years that lead passes the placental barrier (Ballantyne 1902). The maternal blood lead level which might be associated with toxicity to the foetus should therefore be based on paediatric studies where figures between 40 and 60 µg./100 ml. are now regarded with suspicion (Moncrieff, et.al. 1964). Much higher levels are accepted in industry for adult males. A firm paediatric diagnosis of lead poisoning is probable with blood lead figures of 50 µg./100 ml. (Shrand 1961), whereas Kehoe (1961) maintains that in industry there is no "poisoning" below the level of 80 µg./100 ml. Three of the four maternal blood lead estimations in this case gave results above 50 µg./100 ml.

Maternal blood and urine lead estimations are not usually done in cases of stillbirth and it is difficult to find comparative information. Lane (1949) records three stillbirths out of fifteen pregnancies

in a group of women who had been exposed to a low industrial concentration of lead. Their employment had been terminated as soon as they were discovered to be pregnant. The lead in urine of men who had been working side by side with these women previously varied between 0.075 mg. and 0.125 mg. per litre with a mean of 0.09 mg./litre. It is of interest to note that this Innerleithen patient, a week after an intra-uterine death of foetus, had a urine lead of 0.086 mg./litre. The carbon dioxide combining power was just outside the normal laboratory range of 24 to 34 m-equiv./litre.

Toxic effects of lead on the kidneys of young children are well recognised, owing to the work of Nye (1933) in Australia. One of the principal toxic effects of lead is on blood formation and the pathologist specifically mentioned the bloodless condition of the foetus, but it is unfortunate that maceration made study of the foetal blood impossible. The maternal blood lead level, plus the raised lead content of the foetal kidney compared with adult normals provide grounds for stating that this stillbirth was associated with unusual lead exposure. If this is accepted, then the comment that the pink fluorescence of coproporphyrin in urine is an early means of estimating lead damage would appear to be fully justified. However, seventeen of the twenty-four patients delivered during the first year reached or passed the Donath level of 2½. While this appears to be a sensitive indicator of possible danger, it is not inevitably followed by disastrous consequences. The ineffectiveness of punctate basophil counts at this level of exposure is quite clearly shown.

Punctate Basophilia and Raised Urine Coproporphyrin Level with Normal Baby.

Case No. Mat.6., Mrs. I.C., Age 22 (Para 1).

32 weeks - This patient had felt no foetal movements. X-ray showed no abnormality of the foetus. She was seen by a Consultant Obstetrician who confirmed that the uterus was of the size to be expected for this stage of pregnancy with a cephalic presentation and that no foetal heart could be detected.

No special significance is attributed to the absence of foetal heart sounds or movement. It is merely recorded as an unusual phenomenon to be detected so late in pregnancy.

33 weeks - She felt life for the first time and on the following day the foetal heart was heard.

Pregnancy continued for two weeks beyond the expected date and labour was induced in hospital by intravenous "syntocinon infusion". She delivered spontaneously a normal 7 lb. 12 oz. baby.

Urine Coproporphyrin Results in Pregnancy (Donath apparatus)

Weeks of Pregnancy	Before 28	29 - 32	33 - 36	37 - 40+
Results on Donath Scale	2	1, 1, 1, 2½	1, 1, 3½, 2, 4	2, 3½, 3½, 4½, 2½, 1, 2½, 2½
Glycosuria:				
Clinistix			+	+ + + + + + +
Clinitest			¼	

36 weeks - (A week after the Donath reading 4 was obtained) Hb 12.4 g./100 ml. Blood lead 36 mg/100 ml. Punctate basophilia present 0.6%

Treatment: This patient was given Ostocalcium tablets (Calcium phosphate 325 mg., calcium sodium lactate 162 mg., Vitamin D (Calciferol) 500 units) two, three times per day. She was also told to drink more milk and much less tea and water. Treatment with the Chelating agents used in industrial medicine is contra-indicated in pregnancy because these are known to produce foetal malformations. (Tuchman-Duplessis and Mercier-Perot 1956).

Increased Urine Coproporphyrin Excretion with Congenital Abnormality.

Case No. Mat.7, Mrs. D.L., Age 23, (Para 1).

This patient had an uneventful pregnancy and a spontaneous delivery at term of a 7 lb. 2 oz. girl, who appeared normal at birth. She was attending for antenatal care at the same time as Case No. Mat.6 and lived in the house next to her. Mrs. D.L. was due to be confined one month before Mrs I.C. (but the latter, as already mentioned, was induced a fortnight after her expected date of confinement). This patient showed increased urine coproporphyrin at the same time and samples were taken for blood lead estimation from both patients on the same day. Both patients showed a low grade glycosuria (¼%)

19 weeks - Hb 12.1 g./100 ml. No punctate basophils seen.

40 weeks - Hb 11.8 g./100 ml. No punctate basophils seen
Blood lead 31 µg./100 ml.

Urine Coproporphyrin Results in Pregnancy (Donath apparatus).

Weeks of Pregnancy	before 28.	29-32	33-36	37 - 40+
Results on Donath scale:	-	2, 3	3	2½, 2, 3½, 3½, 3½
Glycosuria - Clinistix				+
Clinitest				¼

Eight months after delivery when this child was attended for treatment of a pharyngitis she was found to have a very marked nystagmus. She had, prior to this time, had three injections of Triple Antigen (Diphtheria, Pertussis, Tetanus Vaccine), had been vaccinated against Smallpox, and had two doses of oral Poliomyelitis Vaccine. Her fundi were examined under anaesthesia by a Consultant Ophthalmologist who considered, because of her very poorly pigmented fundus that she was a partial albino. The rest of the fundi were normal and in particular, the optic discs were normal. He was in no doubt that this was a congenital defect. She also

developed a small haemangioma in her left frontal area and subsequently a left internal strabismus. There is no family history of albinism in this case.

Discussion on Cases 6 and 7.

Since there are other causes of coproporphyrinuria this can only be attributed to lead conclusively if there is supporting evidence such as punctate basophilia or a raised blood or urine lead content. In Case 6, the punctate basophilia gave valuable confirmation that the unusually high urinary coproporphyrin excretion was due to lead. In Case 7, there is no such confirmatory evidence. Hepatic dysfunction and congenital phorphyrias have not been excluded. The coincident occurrence of the two cases at the same time, however, does give some support to the presumption that the raised urine coproporphyrin levels in Case 7 were due to lead.

The incidence of albinism was eight and of congenital nystagmus nineteen cases out of 9,951 children with congenital defects in the recent College of General Practitioners Survey of Congenital Abnormalities (Slater 1964). Waardenburg, Franceschetti and Klein 1961 give the frequency of Albinism for Scotland as about 1 : 21,000 (Fewer in England, Glasgow 8 : 100,000). Of three well defined types of partial albinism (Hsai 1960) two are simple dominants and the third is a sex linked recessive affecting males only - and this is a female child. If we accept Hsai's statement that every inborn error of metabolism may possibly represent a fresh mutation, then such an abnormality associated with a positive result from an ante-natal toxicity test merits special consideration. Lead is a known teratogenic agent (Nishimura 1964). Partial albinism is due to a failure of synthesis of Tyrosinase, a copper containing oxidase required for the conversion of tyrosine to melanin (Stanbury and Wyngaarden 1960). Lead is not

included in a range of chemical substances listed by Lerner and Fitzpatrick (1950) as inhibiting melanin formation in vitro and in vivo, but copper is essential for normal pigmentation in mammals. While the interference of lead in iron metabolism is well known, studies with copper seem to be limited to the observation that lead can displace copper from the Sulphydryl groups of bovine serum albumin (Klotz, Urquhart and Fies 1952). It is obvious that no definite conclusion can be reached on the origin of this particular partial albinism, but further studies on this interference in copper metabolism produced by lead might be rewarding.

Punctate Basophilia and Premature Labour.

Case No. Mat.8, Mrs. M.L., Age 30, Primipara.

This patient had a six year history of sterility and had full sterility clinical investigations. The result of these investigations was reported as follows: "insufflation of the tubes showed normal patency. Endometrial biopsy proved normal ovarian activity, but the post-coital test was poor until we advised alteration in posture when the result was very good indeed."

Conception occurred seventeen months after these investigations.

10 weeks - Hb 12.9, E.S.R. 12 mm. in 1 hour. No. punctate basophil cells seen.

11 weeks - Had a threatened miscarriage. This settled down with rest in bed at home and morphine initially to ease her pains.

27 weeks - She began complaining of heartburn and then anorexia and showed glycosuria positive to Clinistix test but negative to Clinitest.

31 weeks - Routine blood examination showed haemoglobin 10.9 gm./100 ml. E.S.R. 58, Punctate basophils present 0.4%

33 weeks - This punctate basophil count was repeated - stippled cells present 0.3%. Blood sugar 2 hours after 100 gm. carbohydrate meal 88 mg./100 ml.

35 weeks - She was admitted to the Western General Hospital with a false labour but with rest and sedation she settled down and she was discharged four days later.

38 weeks - She went into labour and delivered spontaneously a 5lb. 10 oz. baby, which appeared normal at birth, but has subsequently developed three angiomata, one of them a large one on the abdomen.

Water restriction was recommended to this patient at fifteen weeks after her threatened miscarriage. Eleven urine coproporphyrin tests on the Donath apparatus done throughout pregnancy gave readings of 1 (0-50 µg./litre.)

Pre-Eclamptic Toxaemia with increased Urine Coproporphyrin.

Case No. Mat. 9. Mrs. A.W., Age 18, Para 1.

This patient showed systolic hypertension and traces of albumin in the urine from the thirteenth week of pregnancy and at the fifteenth week B.P. 166/80 was recorded. She had dizziness and headaches. She was treated with Amylobarbitone and rest, but continuously showed a systolic blood pressure of 140 from twenty weeks to thirty-three weeks. The diastolic reading was in the range 70 to 80. She had traces of albumin in the urine on a number of occasions, but no oedema.

37 weeks - She was confined completely to bed, B.P. 142/94, albuminuria 100 mg./100 ml., glycosuria ¼% and a urine coproporphyrin reading Donath 3 (100-200 µg./litre).

Since it seemed probable that this increase in urine coproporphyrin could be a hepatic toxaemic effect a full range of liver function tests was done.

Laboratory investigations:

Hb 12.4, P.C.V. 36, M.C.H.C. 34, E.S.R. 22 mm. perlhour. W.B.C. 6,400, Neutrophil 73%, Lymphocyte 24%.
Blood film - no punctate basophils seen.
Blood sugar 2 hours after 100 g. carbohydrate 60 mg./100 ml.
Bilirubin: 0.2 mg./100 ml.
Alkaline Phosphatase: 17 units (K.A.)/100 ml.
Thymol Turbidity: 2 units.
Zinc Sulphate Turbidity: 3 units.
Total Protein: 4.6 g./100 ml.
Albumin: 3.1 g./100 ml.
Globulin: 1.5 g./100 ml.
S.G.O.T: 18 units/ml.
S.G.P.T: 13 units/ml.

In addition to Amylobarbitone, she was treated with Neo-Naclex (Bendrofluazide) and with bed rest her B.P. fell to 120/80. The oedema cleared and the albumin was reduced to a trace. There was no further glycosuria. Facilities for blood lead estimation were not at this time available.

Urine Coproporphyrin Results in Pregnancy (Donath apparatus).

Weeks of Pregnancy	Before 28	29-32	33 - 36	37 - 40+
Results on Donath Scale	1,1,1,2,2,1,1,1	1,1	1,1½,1,1	1½,3,2½,2½,1½,2½,2

This patient has had a further pregnancy after the end of the two year study. She had removed to another house and water restriction was recommended at five months, where there was no water restriction in the whole of her previous pregnancy. Four urine coproporphyrin urine estimations were done on the Donath apparatus between seventeen weeks and thirty-one weeks and all these gave readings of 1 on the Donath scale (0-50 µg./litre).

Comment on Case 9.

Apart from a slight rise in alkaline phosphatase and a lowering of plasma proteins, especially albumin, the

liver function tests are normal. The rise in urine coproporphyrin occurring at the same time as the exacerbation of her toxaemia could suggest that they had a common aetiological factor. A much simpler possibility, however, which was not considered at the time was that increased urine concentration could play some part in this apparent rise in urine coproporphyrin since it was estimated in µg./litre on spot samples and not on 24-hour urine samples.

Anaemia with rise in Urine Coproporphyrin

Case No. Mat.10., Mrs. S.P., Age 23, Primipara.

13 weeks - Hb 12.4 g., P.C.V. 40, M.C.H.C. 31, W.B.C. 8,400, E.S.R. 8 mm/hr.
Film - no stippling or other abnormality seen.

17 - 23 weeks - B.P. readings were 140/90 with no albuminuria or oedema, but thereafter rather lower figures prevailed, in the range 120 to 130/70 to 85.

The routine urine coproporphyrin tests gave a Donath reading 3 at 37 weeks and Donath reading 3½ at 38 weeks.

Blood lead analysis was not at this time available, but blood samples were taken for haemoglobin estimation and punctate basophil counts. This revealed a fall in haemoglobin previously unsuspected, because the patient was normally pale and no alteration in her appearance had been noted. There was no history of any blood loss.

38 weeks - Hb 9.5 g./100 ml., P.C.V. 30, M.C.H.C. 32, R.B.C. 3.72 ml./c.mm., M.C.V. 81, Retic. 2%, E.S.R. 54 mm./hr., W.B.C. 7,650/cu.mm. Normochromic, normocytic red blood cells. White series N.A.D.

Because she was so near term she was treated with intramuscular iron injections.

39 weeks - Hb 9.1 g./100 ml., Retic 3.6%.

40 weeks - Hb 11.3 g./100 ml, P.C.V. 34, M.C.H.C. 33, R.B.C. 4.08 ml./c.mm., M.C.V. 83, Retic. 7%, E.S.R. 49 mm./hr. W.B.C. 9,300. Film: well filled red blood cells showing an anisocytosis, but no other abnormality. White series N.A.D.

The patient went into labour ten days after her expected date of delivery and had a spontaneous delivery of a 7 lb. 5 oz. baby.

Urine Coproporphyrin Results in Pregnancy (Donath apparatus).

Weeks of Pregnancy	Before 28	29-32	33-36	37 - 40+
Results on Donath Scale	2, 1½, 1	1, 1, 1	2, 1½, 2	3, 3½, 3½, 3½, 3½

A blood sample was taken a few days before this patient went into labour and was held over until blood lead estimation again became available.
Blood lead 24.6 µg./100 ml. (Lab.G.)

This baby was normal at birth, but at three months became very miserable with swollen and markedly pink hands. This episode seemed very like pink disease but there was no history of administration of mercury compounds. It lasted four weeks and was treated with increased salt intake and antihistamines. Recovery was complete. At six months the baby developed an infantile eczema which persisted for five months in varying degrees.

Pregnancy with water supply containing 1 p.p.m. lead.

Case No. Mat.11, Mrs. E.J., Age 22.

This patient had an uneventful pregnancy and spontaneous delivery at term of a normal 6 lb. 15 oz. baby. She had nine urine coproporphyrin readings of 1 on the Donath apparatus after water restriction and increase in milk was recommended and one reading of 2 on the

Donath scale prior to that. The character of her water supply only came to light when she complained of the discolouration of her baby's face cloth by copper staining, which has already been illustrated (page 35). As a result of this, water samples were taken which demonstrated, on two occasions, a lead content in excess of 1 p.p.m.

The patient was breast feeding and was able to supply samples of breast milk for lead analyses and these have already been quoted (page 96). Her urine coproporphyrin level rose to 3½ on the Donath scale but she showed no punctate basophilia (Hb 14.9 g./100 ml.) She had been drinking about three pints of water per day and only taking milk in puddings. This change in the pattern of urine coproporphyrin excretion between pregnancy and lactation is very striking. Blood and urine lead estimations were done for this patient and her husband.

Blood Lead:	Mrs. E.J.	Mr. J.J.	(Lab.G.)
	48.69 µg./100 g.	52.54 µg./100 g.	
	Normal 22.9 ± 8.2 µg./100 g.		
Urine Lead:	Mrs. E.J.	Mr. J.J.	
	72.5 µg./litre	130 µg./litre	
	Normal 23.3 ± 12.5 µg./litre.		

This patient had a blood lead level of 2.16 µg./100 g. at twelve weeks in her second pregnancy. The only symptoms of which she complained during lactation were nightmares and weight loss of 6 lbs. during six months of breast feeding.

These patients were tenants of a farm cottage and shared a water supply with the farmhouse. The lead content of this water seemed so high that the Medical Officer of Health was specially asked if he would take action to secure its improvement. The farmer displayed to a considerable degree the irritability and unco-operativeness which Jones (1935) listed among the

features of increased lead absorption. The Medical Officer of Health's right to inspect the supply and take samples was challenged and in the end the only remedy adopted was that the tenants of the cottage were told to draw their water supply for drinking purposes from another part of the farm buildings which received water from a different spring. This cannot be described as a very satisfactory solution. Though the occupants of the farm were also patients of this practice they refused offers of investigation to ensure their own safety since they were sharing this undesirable supply. In this particular instance, the lack of adequate legislation and of established standards applicable to this country proved a very considerable disadvantage, both to Medical Officer of Health and to general practitioner.

Congenital Anomalies.

In Case No. Mat. 2 the baby had a large raised cavernous naevus (strawberry mark) on the arm. The baby of one of the two defaulters from the water restriction regime had a large and unsightly angiomatous formation on the inner aspect of the left thigh. A similar large angioma on the abdomen and two smaller ones on chest and head were noted in a baby whose mother had a punctate basophilia. Because of these observations, all such birthmarks reported by the mother or noted in the course of routine examination in babies from this two year study have been recorded and photographed. In the table which follows all the anomalies relating to this series have been listed along with the maximum ante-natal urine coproporphyrin reading. The positive punctate basophil count in one patient and the blood lead estimation in another have also been included and a note has been made of whether or not the patient was in the group subject to water restriction. Infantile eczemas have not been included.

Congenital Anomalies Associated with the Innerleithen Two Year Maternity Study

Initials	Anomaly	Punctate Basophilia Recorded	Maximum antenatal urine coproporphyrin Donath Reading	Blood lead µg./100 ml.	Water Restr. Group
L.D.	Angioma		3½		± (Defaulter)
C.L.	Three Angiomata	0.4%	1		+
S.L.	Congenital Nystagmus Partial Albinism and Angioma		3½	31	
K.W. (lives above S.L.)	Angioma		2		
E.G.	Angioma		3		+
T.S.	Angioma		2		+
E.P.	Congenital dislocation of hip.		1		+
S.B.	Labial Fusion		1		
N.W.	Skull deformity and Hydrocephalus		2½		+

Out of the total of seventy-seven pregnancies in the period of the study, thirteen have since left the practice area. There were two stillbirths, one of which has been described and the other resulting from a severe pre-eclamptic toxaemia.

There was one neonatal death after six hours - the baby of a well controlled diabetic, who was induced in hospital at thirty-eight weeks.

This series of anomalies is, therefore, drawn from sixty-one babies surviving and remaining in the practice, giving an incidence of 15% This is reduced to 6.6% if the angiomata are excluded.

Illustrations of Congenital Anomalies.

Case Mat 8:- Baby C.L. at 1 year to show relationship between size of haemangioma on abdomen and size of baby. The mother had Punctate Basophilia 0.4% in this pregnancy

Case Mat 8:- Baby C.L. at 2 years - showing increased blanching in the centre of the haemangioma. There appears to have been some shrinking. The two smaller haemangiomata - below the right breast and in the scalp had by this stage decreased in size and almost disappeared.

Case Mat 4:- Baby L.D. Haemangioma on inner aspect of left thigh. Mother defaulted from water restriction recommendations. Maximal Maternal Urine Coproporphyrin Reading: 3½ on Donath Scale.

Baby E.G. Haemangioma on scalp - Maximal Maternal Urine Coproporphyrin Reading: 3 on Donath Scale.

Case Mat 7:- Baby S.L. at 2 years 11 months. Haemangioma of forehead. Also has Congenital Nystagmus, Strabismus, and Partial Albinism affecting the eyes. It will be noted that the hair is golden in colour, not white. Maximal Maternal Urine Coproporphyrin Reading: 3½ on Donath Scale.

Baby K.A.W. Haemangioma. This patient lives in the flat above Case Mat 7 (S.L.)

Baby T.K.S. - Haemangioma of left upper arm.

Baby S.B. - Labial fusion at 1 year 7 months prior to operative separation. There was no abnormality of the underlying structures.

Baby E.P. - Congenital dislocation of hip - X-ray taken soon after birth.

Baby N.W. - 1 year 6 months, has a marked skull deformity with prominent right frontal and left parietal areas and depression of left frontal area. This has produced a twisting effect on the whole skull and when seen from above the ears seem unequally placed, the right being further forward than the left.
(A.P. view - lateral view appears overleaf).

Baby N.W. - 1 year 6 months - Skull: lateral view.
The radiologist's report: "There seems to be a degree of hydrocephalus with probably an increased convexity of the left partial region and some widening of the sutures.

Comment on Congenital Anomalies.

Baird (1962) gives an estimation that 10 per cent. of malformations can be attributed to virus infection, less than 20 per cent. to known mutant genes, and less than 10 per cent to the newly described chromosome mutations. This leaves more than 60 per cent. still unexplained. In many of these there may be a complex interaction of genetic and environmental influences.

The group of anomalies which have been listed were compared with the results of the ante-natal screening of urine samples on the Donath apparatus. The coincidence was noted that three of the pregnancies which had angiomas had readings of 3 or $3\frac{1}{2}$ on the Donath scale. Of the thirty-six patients who had a Donath reading of 1 throughout pregnancy, the only one whose baby developed an angioma, was the patient in whom punctate basophilia was recorded.

Willis (1962) defines angiomas as non-neoplastic malformations of vascular tissue development. He states that heredity plays little part, if any, in the causation of skin haemangiomas. Nishimura (1964) quotes Weiker, et.al. (1962) as listing haemangiomata of nose and upper lip among the patterns of foetal thalidomide damage but the reference given is incorrect, referring only to limb deformities and making no mention of this detail.

Ingalls, Tedeschi and Helpern (1952) describe the development of neovascular and angiomatous tissue in the eye as a characteristic part of retrolental fibroplasia which is associated with abnormalities in the oxygen supply to premature babies. The angiomata in the present series can only be described as interesting coincidences which should be borne in mind in any future screening programme for lead effects in pregnancy.

The case of congenital nystagmus and partial albinism has already been discussed with the maternity case history. I have not noted any reference to an association between congenital dislocation of hip and any drugs or toxic agents, but labial fusion has been recorded by Wilkins, Jones, Holman and Stempfel (1958) and by Liebow and Gardner (1960) following treatment with progesteroids in the early weeks of pregnancy. In the present case, there was no hormone treatment of any kind. The only features noted in early pregnancy were an injection of poliomyelitis vaccine twelve days after the beginning of her last menstrual period and a course of penicillin for an attack of tonsillitis which occurred when she was eight weeks pregnant.

The skull deformity is quite marked and though the radiographs demonstrate the abnormal size of the head they do not show very clearly the distortion produced by enlargement of opposite frontal and parietal areas. Ballantyne (1902) quotes a description by Rennart in 1881 of the children of workers glazing pottery who were suffering from lead poisoning. The heads of the infants were in many instances noted to be square shaped with very evident "tubera frontalia et parietalia". The heads increased rapidly in size but the fontanelles were not larger than usual, the sutures did not gape and the orbits and position of the eyeballs were normal. These macrocephalics were noted in eighteen out of nineteen pregnancies if both parents were suffering from lead poisoning (the remaining child being stillborn). If the mothers were only slightly affected, the incidence was 67 per cent. (eighteen out of twenty-seven) whereas if the mothers were healthy and only the fathers were suffering from lead effects the incidence was 61 per cent (twenty out of thirty-three). This is a good example of the type of

observation which was possible from the abundant clinical material available before the control of industrial lead hazards was well established.

The experience of Oliver (1911) was that the children of potters suffering from plumbism were hydrocephalic and died a few days after birth from convulsions.

The skull deformity in the present case cannot be attributed definitely to lead, however, because the only evidence to suggest it is at the most a very marginal rise in urine coproporphyrin excretion in early pregnancy. There is no supporting evidence available of either punctate basophilia or increased blood or urine lead. The patient had a miscarriage at seven weeks, three months prior to this conception. She had a long period of psychiatric treatment with several admissions to a psychiatric hospital and for eight months prior to the commencement of this pregnancy had been receiving Tryptizol (Amitriptyline Hydrochloride) 25 mgm. twice daily. She also had both Ancolan (Meclozine Dihydrochloride) and Avomine (Promethazine Theoclate), as treatment for vomiting in early pregnancy. In addition, there is a history that an older sister had a minor degree of skull deformity in infancy though there is no evidence of this remaining.

While noting this history of drugs and the possibility of hereditary influences being related to this anomaly, it is nevertheless interesting that from such a relatively small series of seventy-seven patients a congenital abnormality has been found which bears a resemblance to one described last century in association with lead poisoning.

General Discussion on Maternity Cases.

From the evidence which has been given there is no cause to dispute the sensitivity of maternity patients to lead. The appalling obstetric history of the first maternity case with two surviving children out of the first six pregnancies is an echo of some of the historical observations on the effects of lead in pregnancy.

The position of a general practitioner who finds that his water supplies have an aggressive action on lead piping is one of some difficulty. It is very easy to create public anxiety on this subject. In view of the lack of legislation, however, it is difficult to press for expensive water improvements on grounds of medical urgency. There has been in the past a lack of suitable methods for investigating the effects on patients of such small quantities of lead.

The Donath apparatus proved very convenient for this purpose. Since urine samples are brought as a routine during pregnancy, this study was able to be carried out without causing alarm or anxiety to the patients. With this test, however, new standards have to be established and confirmed by long, continuous use. The application of standards of toxicity used in industry, to maternity patients who, as a group, are rigorously excluded from industrial risks because of their extreme sensitivity, is obviously inconsistent. Punctate basophil counts for the most part were not found to be helpful.

Routine urine lead estimation, as practised by some large industrial concerns, was not available but a small number of blood lead estimations were arranged. Modern theories on the deposition and mobilisation of lead and on the changes in the physiology of the blood during pregnancy appear to make necessary

a complete re-assessment of one of the most valuable tools for studying exposure to lead. A comprehensive study of normal blood lead values at the varying stages of pregnancy seems to be indicated.

Several laboratories have helped at times with blood lead analyses, but it has been exceptional to obtain a result in less than three weeks. The Donath apparatus has obvious advantages, as a screening test for the care of pregnant women, giving a result in the consulting room in fifteen minutes.

The objection that the coproporphyrin test is not completely specific and that hepatic dysfunction could interfere with its effectiveness, prompted the examination of a large series of urine samples from a maternity hospital. This gave no evidence to suggest that the disturbance of urinary coproporphyrin excretion was common in pregnancy.

There was a clear difference in the results between the maximum urinary coproporphyrin levels in maternity patients with no water restriction and those who had their intake of water restricted. A similar difference in results was noted between the unrestricted patients and a control series drawn from both groups when no longer pregnant. This may be evidence of the increased susceptibility of the pregnant woman.

The study was extended to other areas to discover if the proportion of patients reaching Donath scale 3 (100-200 µg./litre) in Innerleithen was unusual. Eleven out of thirty-five Innerleithen patients had such results. In the large hospital series, eight out of 404 patients reached or passed this level (2 per cent.). Two of these were in the 400-800 µg./litre range and these grossly abnormal findings exceeded

the highest Innerleithen result. Unfortunately, it was not possible to investigate adequately to find a reason for these abnormalities.

Water supplies of the type found in Innerleithen are not uncommon in Scotland. The Donath apparatus was used by a practitioner in Aberdeenshire in August 1963 to find whether a similar pattern of maternity urine coproporphyrin excretion might occur in other areas with similar water supplies. A series of samples was obtained during that summer from maternity patients on a hard water supply for comparison. The difference between these supports the theory that the urinary coproporphyrin excretion of maternity patients bears a relationship to the water supply.

From the notes and comments on individual cases, it can be seen that only one can be shown to have come to severe harm with definite confirmation of increased lead absorption, but a number of others show disquieting features.

The Donath apparatus has demonstrated the existence of a problem. Previously this had only been suspected. The possibility of widespread toxic effects on maternity patients from traces of lead in water supplies was discussed at length by Porritt (1934) but at that time there was no suitable screening test available. In certain parts of the country where the water supplies are still soft and acid such tests could easily be added to the routine of ante-natal care. They could indicate the need for much more detailed investigations. As found by Zielhuis (1961), coproporphyrin results have been most valuable in group studies. With single cases the test is not infallible.

Observations on Other Conditions

Pernicious Anaemia: In 1961, there were in the practice eight cases where this diagnosis had been made and confirmed by sternal marrow examination. There were in addition, two frail elderly patients to whom this diagnosis had been given prior to my arrival in the practice, but who were too infirm to be sent to hospital for investigation. Several of these have died and the known proved cases in the practice at present are six in number. Thus the incidence has ranged from three to four per thousand patients in the practice.

In a College of General Practitioners survey of the prevalence of this disease in Great Britain (Scott, 1960) [redacted] covering a population of over sixteen million persons, the national incidence was found to be 1.27 per 1,000. The prevalence rate for Scotland was 1.80 per 1,000 and for England as a whole 1.19 per 1,000. The highest rate recorded was 2.46 per 1,000 in Banff and Elgin.

Little significance can be attached to a high incidence of a disease in one practice where such small numbers are involved. Reference is made to this only because Lourau (1946) has demonstrated a disappearance of the antipernicious anaemia factor in rabbits fed with lead and suggests that this is due to an inhibition of synthesis of the factor.

Multiple Sclerosis: Throughout these studies the practice incidence of this disease has been two per thousand (four patients). One patient died at the time when another case was diagnosed. All have been confirmed by a Consultant Neurologist. McAlpine, et.al. (1955) give prevalence rates from field surveys as rates per ten thousand with a range from 1.04 to 6.58. The latter figure refers to a survey in the North of Scotland.

There is, therefore, a high incidence of Multiple Sclerosis in this practice but the small number of patients involved makes this observation of very doubtful value.

Attempts have been made in the past to link abnormal lead intake with Multiple Sclerosis (Campbell, et.al. 1950) and to disprove this possibility (Butler 1952). Warren (1961) stated that in areas where the incidence of Multiple Sclerosis is high, the geochemical background suggests the presence of greater amounts of lead in the earth's crust than may be considered to be normal. An attractive hypothesis could certainly be made out for mobilisation of stored lead as a factor in a recurring neurological illness. Fatigue and infections are both associated with relapses in Multiple Sclerosis and are also described as precipitating factors in lead poisoning. An opportunity presented for clinical observations on this point with one patient.

CASE M.W. Female, age 40.

This patient's water supply has already been mentioned (House E). It was on Innerleithen Burgh water supply and the highest lead content obtained from it was 0.36 p.p.m. after heavy rainfall. Because of this an ion exchange resin filter was fitted. Some time after this had been installed, the patient developed vague abdominal discomfort and nausea. In view of the previous history of this water supply, blood samples were taken for haemoglobin and lead estimation and blood films were made which showed no stippling, (haemoglobin 12.3 gms.).

A week later she was wakened by a severe abdominal colic followed by diarrhoea and severe vomiting. The colicky pains persisted all day and the diarrhoea recurred in the evening. On the next day there was diarrhoea in the morning and persisting

very severe colic for the whole day with no further stools. Temperature 100° was recorded on the second evening. There was extreme tenderness over the colon on palpation to such a degree that a consultant surgeon was invited to see the case. She was being treated with "Streptotriad" as an acute infective gastro-enteritis. Because of the filter and of the pyrexia lead seemed improbable as a cause of this illness but further blood films were taken on the first and third days of the acute attack and both showed stippled cells present less than 0.2%. Stool examination showed no intestinal pathogens and virus culture was likewise negative. The samples were taken prior to the treatment with "Streptotriad". Blood lead estimation at the time of the vague premonitary symptoms: 130 µg/100 ml. (Lab. P.*) . On the first day of the acute illness 165 µg/100 ml., and on third day was 329 µg/100 ml. A 24-hour urine sample was taken during the third and fourth day of the acute attack: 221 µg/24 hrs.

These blood and urine lead levels, in association with an acute attack of what can only be described as colitis with marked colic would appear to be diagnostic of lead poisoning, but it must be noted that Mokranjac and Soldatorri (1958) report an increase in the blood lead level resulting from treatment with Streptomycin.

When the patient was seen on the morning of the acute attack, the possibility was considered that the filter might fail if the water was run through it too quickly. Three samples were taken in the middle of that forenoon, the first without the filter, and the second and third after fast and slow filtration. The figures have already been given in the section on

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* Lab. P. - Laboratory of Borders Hospital Group, Peel Hospital, Galashiels.

water supplies. The unfiltered mid morning sample had a lead content of 0.289 and this was reduced by filtration to 0.06 if the water passed through the filter slowly or 0.07 if the water was run through the ion exchange resin filter as fast as possible.

At that time, the possibility of different effects from different compounds of lead in water supplies had not been considered. It has since been appreciated that the lead passing through the filter at that time might well have been in the form of salts of humic and fulvic acids as already described, so that the lead which was passing through the filter was in the form most likely to be converted into lead chloride in the stomach.

Mobilisation of previously stored lead by Streptomycin might have affected the last of the blood results but could have no influence on the first two blood lead estimations. These therefore give grounds for suggesting that lead in some forms occurring in water supplies at a level of 0.07 p.p.m. may be capable of causing acute gastro-intestinal irritation associated with blood lead levels which would merit the title "lead poisoning".

This patient had a known Multiple Sclerosis of eight years' duration.

Shortly after this episode, she developed a bilateral "wrist drop" - weakness of extensors of both wrists, the right being worse than the left. She was seen by a Consultant Neurologist who confirmed that she had physical signs of both Multiple Sclerosis and Lead Poisoning.

This house was subsequently equipped with a polythene piped water supply from the main.

Three years after this episode she was given a course of treatment with Achromycin for a urinary infection and four days later developed a very acute

attack of vertigo and a unilateral flaccid lower limb paralysis. In the paper by Mokranjac and Soldatorri (1958) already mentioned, a rise in blood lead level in previously poisoned sheep from 220 to 720 µg/100 ml. was recorded after a six-day course of Terramycin (Oxytetracycline) in a dose of 5 G. per day by mouth. This patient was receiving Achromycin (Tetracycline) in a dose of 1 G. per day, but in view of her previous history of lead poisoning, and the suddenness and severity of her attack, blood was taken for lead estimation and treatment was started with Penicillamine 150 mgms. four times daily. Blood lead estimation on the day after the onset of vertigo was 9.79 µg/100 G, (Lab.G.); a week later after completion of five days on Penicillamine, it was 0.3 µg/100 G.

On the recommendation of a Consultant Neurologist this patient was subsequently treated with Prednisolone: initially 60 mgms. per day with gradual reduction down to a maintenance dose of 10 mgms. per day. After this treatment had been continuing for three months another blood lead estimation was arranged and on this occasion no lead was detected, i.e. 0 µg/100 ml. blood.

In this case, therefore, despite a known history of previous lead poisoning, there was no evidence of abnormal blood lead level in a patient with Multiple Sclerosis at the time of an acute exacerbation. There was also no evidence of lead mobilisation from treatment with Achromycin (Tetracycline). Treatment with Penicillamine was associated with a fall in the amount of lead which was present in the blood and which was already below the normal range for the laboratory concerned. Prolonged treatment with Prednisolone produced no lead mobilisation. It would be unwise to generalise in a condition like Multiple Sclerosis from observations of a single relapse in one case but there are a number of unusual features in this instance.

Lead Content of Neurological Tissues.

Motor Neurone Disease.

A patient with a progressive neurological disorder was diagnosed as suffering from Multiple Sclerosis and this diagnosis was confirmed first by a Consultant Physician and later by a Neurologist. Blood lead estimation in the early stages was 44.5 µg/100 ml. (Lab. P.) and blood film showed no punctate basophilia. His condition deteriorated progressively without any intermission and he died within three years of the onset. Post mortem and microscopic changes were those of Motor Neurone Disease. There was no evidence of Multiple Sclerosis.

Lead Content of Brain - 0.009 mg/100 G. (Lab.N.)
(Normal 0.01-0.09).

Lead Content of Spinal Cord - 0.006 mg/100 G.

This patient was apparently given treatment with Penicillamine in the terminal stages of his illness though there seems to have been no clinical or biochemical reason for this. The brain result is low and in marked contrast to the results from the dogs which have been mentioned.

Vertigo.

The first observation on this subject was made by the Senior Consultant Ear Nose and Throat Surgeon, at the Royal Infirmary, Edinburgh. He wondered if there could be some unusual vitamin deficiency in Peeblesshire and wrote to my predecessor asking for information. The letter came to light when the patient attended for a different complaint in 1961.

COPY

Wards 39 and 40,
The Royal Infirmary,
Edinburgh.

25th January 1954.

Dear Dr. Flett,

Mr. A.B. (52), A.H., Traquair.

This man has Meniere's disease in the right ear. He has all the characteristic signs of giddiness, nausea and vomiting and rotational vertigo. The tests confirm this impression, and I think the best thing to do would be to bring him up here into the ward to start treatment, do some more tests, and have x-rays taken.

It is extremely interesting to me to see how many cases of this particular disease we get from the Innerleithen and Peebles district. There are indeed so many that it does not seem to be possible that it is pure coincidence. Even the nursing and clerical staff now remark, "another from Innerleithen or Peebles" as the case may be.

Have you noticed in your practice a very large number of these patients? Possibly of much slighter degree than this man. I shall be extremely interested if you can find time to drop me a note about this.

Yours sincerely,

(signed) Dr. I. Simson Hall.

When enquiries were made of one of the local plumbers about which houses in the area were supplied with unusually long lengths of lead pipe he mentioned this particular house and suggested that at one time the water supply had been carried by almost a mile of lead pipe. As a result of frequent bursts much of this had latterly been replaced by copper piping.

Transient attacks of vertigo are not uncommon in this practice but "giddiness" is a vague symptom which may be associated with a great number of different conditions. Some attacks are recurring and associated with progressive deafness, but it has not been possible to estimate serial blood lead levels in such patients during attacks and between attacks.

Two adult males with incapacitating acute attacks of vertigo had blood lead estimations done.

One of these patients (I.C. Male, age 41) occupied the house "M" to which reference has already been made in the section on water supplies, page 70. This house showed a maximum lead content of water supply of 0.32 p.p.m. after heavy rainfall. There was no mains tap, all water passing through a lead lined storage cistern, but this was not discovered till after the acute vertigo. The water supplies were investigated because it seemed likely that the house would have a long lead pipe supply system. The patient had occupied the house for ten years and when enquiries were made at the time of taking of the water samples it was discovered that both occupants, husband and wife, were subject to what they described as "chills" in the stomach. They were invited to ask for medical advice on the next occasion when they had an attack of this sort.

The next attack consisted of abdominal discomfort, preventing sleep, lasting from 1 a.m. to 3 a.m. in the case of the husband and from 1 a.m.

to 5 a.m. in the case of the wife. The wife also complained of nausea and eructations. She felt that her memory had deteriorated over the last three years, and in these three years had four attacks of difficulty in focusing her vision lasting for five minutes only, the last of these having occurred two days previously. The husband, apart from his generalised abdominal discomfort, had a previous history of intermittent headaches but no other complaints.

Laboratory findings at the time of this mild gastro-intestinal upset (Lab. P.) -

	Husband	Wife
Hb	14.3 G/100 ml.	13.1 G/100 ml.
W.B.C.	4,850	6,550
Stool micro	N.A.D.	N.A.D.
Culture	No intestinal pathogens isolated.	No intestinal pathogens isolated.
Blood Film	N.A.D.	Very occasional stippled cells seen. No other abnormality.
Blood Lead	111.5 µg/100 ml.	130 µg/100 ml.
Urine Lead	-	205 µg./litre 313.7 µg./24 hrs.

Rainfall: Following a spell of dry weather a rainfall of 0.24 inches occurred three days previous to this attack.

After this episode these patients were advised to run the kitchen tap for at least five minutes each morning to displace the water lying in the lead pipes overnight.

Four months later the husband developed an acute attack of vertigo with sudden onset on waking at 7.30 a.m. He staggered about when attempting to go to the toilet and vomited. He had a feeling of anti-clockwise rotation. He had slept well and had no

other complaints than vertigo and nausea.- no headache and no abdominal pains.

On examination he was found to have a well marked nystagmus to the right. He had no disorder of hearing, and no other abnormality was discovered. He was treated with Stemetil (Prochlorperazine Maleate) 5 mg. T.I.D. and the vertigo subsided till 6 o'clock that evening, when it recurred very severely for three hours with further vomiting and one normal stool - no diarrhoea. Since the water supply to this house had already been investigated for lead content, blood was taken for stippled cell count and blood lead estimation and the collection of a 24-hour urine output arranged. On the following morning he was feeling better with no vertigo at rest in bed, and the nystagmus was less marked.

By the third day he was well enough to be allowed up for a short time. On this day, a slight difference in hearing was noted - there was a difference of 2-3 inches in range of hearing of a watch ticking - the right being impaired. This was the only occasion on which this was noted despite daily testing.

On the fourth day he was further improved, but the blood lead and 24-hour urine were repeated.

Laboratory Results (Lab.P.)

Day 1	-	Blood Lead	30 µg./100 ml.
" 2	-	24-hour Urine	108 µg./24 hrs.
" 3	-	Blood Lead	418 µg./100 ml.
" 4	-	24-hour Urine	377 µg./24 hrs.

Haematology

21/9/61 - No stippling seen.
24/9/61 - do.

Two dogs are kept at this house and one of these had diarrhoea on the night before and the morning of his master's acute vertigo. This dog had been kept in the house. The other in a kennel outside was not

affected. It had water from an outside tap and not from the house.

Blood lead analysis from dog with diarrhoea - 115 µg./100 cc. (Royal (Dick) Veterinary College).

After this episode, it was discovered that this house had no mains tap but that all the water passed through the storage tank in the roof which was lead lined.

Rainfall previous to this episode: Very heavy rainfall 46 mm. fell nine days prior to this attack of vertigo and 12 mm. of rain fell six days before to this attack. This episode was in September.

Since the wife was a trained dietician, use was made of her services to prepare a diet of the type and quantity which her husband would eat for a 48-hour period. The results of lead analyses of this diet have already been given and discussed. They showed that this patient was obtaining from diet alone an amount of lead which just exceeded the level Kehoe gives as a limit for safety (o.606 mgm. compared with 0.6 mgm. per day). To this must be added a lead intake from his water supply which amounted to 0.221 mgm. per day from the sample which was sent containing 0.13 p.p.m. This could be expected to rise to 0.544 mgm. per day at times which the water supply reached its peak level of 0.32 p.p.m.

One of the interesting features of this case is the rise in blood and urine lead which took place over the course of a few days. I had calculated that if 90 per cent. of the lead was contained in the red blood cells then this incorporation of lead would be likely to take place in the bone marrow and so might not show up in a blood lead sample taken immediately during an acute attack. These results

seem to give some confirmation of this theory. They are, however, subject to the observations on analytical results in general which have been made earlier.

The blood lead estimations from the four dogs which were more consistently raised than any of the other groups were all inevitably taken slightly later than the human samples because of the need for arranging appointments for the dogs to be dealt with at the veterinary college in Edinburgh.

The second patient was W.S., Male, age 55.

This van driver collapsed at the wheel of his vehicle, one afternoon, with an acute vertigo and vomiting. He had no tinnitus and no nystagmus, B.P. 160/100. He was treated with Stemetil (Prochlorperazine Maleate) and improved, but on the following day had another attack with definite nystagmus and a slight trace of deafness in his right ear (an impairment of hearing of a watch tick compared with the previous day). His condition improved rapidly over the next four days and then he had another attack with recurrence of the nystagmus.

Blood examination - Hb 15.4 g./100 ml., punctate basophil count: 0.3%, E.S.R. 1 mm./1 hr.

In view of this punctate basophil count it was repeated and blood was taken for lead estimation eleven days after the initial attack. Repeat blood count - Hb. 15.9 g./100 ml., punctate basophils: 0.6%, E.S.R. 2 mm./1hr., Blood lead: 122 µg./100 ml. Urine lead: 115 µg./24 hrs.

It will be noted that the punctate basophil count doubled in the six days that elapsed between the initial blood film and the blood film taken at the same time as the blood lead estimation.

Urine coproporphyrin estimation was not available at this time and blood lead estimations were severely restricted. It was several weeks before the blood lead result became available, the patient in the meantime had made a complete recovery and no studies of his water supply were made.

General Discussion.

Lead has long been recognised as a toxic agent but many of the observations of previous generations are no longer common knowledge. It was not initially appreciated that it was necessary to go far beyond the literature and textbooks of the last thirty or forty years for information on some of the problems which have been described. For example, obstinate constipation is now regarded as one of the hall-marks of lead poisoning, and this is very difficult to reconcile with an acute gastro-enteritis in which diarrhoea is the commonest symptom. There are however numerous historical references to this, going back to Galen associating Dysentery with lead piped water supplies. The sensitivity of dogs to lead poisoning and the absorption of lead by the sediment in water supplies are other instances where historical observations are of value. The ancient worthies had the advantage of a great abundance of clinical material.

Our modern assessment of the effects of lead is based on laboratory measurements of variations from normal physiology but it is interesting to compare descriptions of lethargy (Porritt 1931) and irritability (Jones 1935) as early features of lead intoxication, with the results of a study by Saitzeva (1953). In experiments with rats he found that lead in daily doses of 0.05 mg/kg. caused no alteration in a range of physiological functions studied, but that amounts over 0.005 mg/kg. affected the nervous system causing interference with conditioned reflexes.

A standard has been established for the limit of the lead content of food. It seems inconsistent that there is no similar standard in Britain for a limit to the lead content of drinking water. The World Health Organisation has an International Standard limit of 0.05 p.p.m. for lead but this has not, as yet, been adopted by this country. There is therefore no established limit for the

lead content of water supplies in Britain. The questions which arise are whether it is necessary to impose such limits and whether the British limit for lead in food, and the International limit for lead in water are adequate.

The validity and stringency of the standards for lead in food and drink must relate to the total burden of lead absorbed and stored, since stored lead is able to be mobilised to constitute a future toxic hazard. We must therefore accept Kehoe's (1961) level for safety for the lead intake of a community of 0.6 Mg. per day. Above this amount measurable storage of lead occurred. He specified this amount over a period of years, but the intake we are considering may be lifelong. Williams (1958) suggested on a theoretical basis that many people might be at the limit of permissible lead intake and certainly the diet analysed for these studies bears this out. It seems that his plea for a more stringent standard for lead in food is justified.

The great variation in the lead content of water is a handicap in the imposing of standards, but Thresh et al (1958) state quite clearly that just as the strength of a chain is that of its weakest link, so the quality of a water supply must be measured by the worst sample which can be obtained from it at any time. The permissible lead content of water must allow for variation in the total intake of water and must also be related to the lead content of the food. In these studies only one diet has been analysed and therefore the average lead content of the diet of the community is unknown. With the diet which was analysed there was no margin whatever for the water to contain lead within the permissible total limit.

There are some difficulties in co-ordination of efforts to reduce lead content of water supplies. Water Engineers and Burgh Surveyors are normally responsible for the treatment of water supplies, and the effectiveness of their work is assessed by Water Analysts. Reports are presented to lay water committees who are advised by the

Medical Officers of Health on the interpretation of the analysts' findings.

Clinical experience of the early effects of lead is for the most part limited to the medical officers of industrial establishments where lead is a hazard, and to University Departments of Industrial Health. Paediatricians are also interested in Plumbism because of the number of children poisoned from chewing at lead painted surfaces but the picture with which they are concerned is usually encephalopathy, which is now rare in industrial medicine. There is no one person concerned with the lead content of the water and the clinical care of the patient. The Medical Officer of Health and the General Practitioner are most involved, but neither is likely to have any great practical experience of the subject in this decade. This may explain some of the difficulties in finding in the literature clear evidence of harm from small quantities of lead in water supplies.

It has been noted with concern that one method of analysis which has been used for over a century is not sufficiently sensitive for estimations relating to the present International Standard limit for lead. The observation has been made that some, but not all, water samples may contain lead in a form which is able to be separated off by distillation. There is a need for further study to confirm this and to discover the frequency with which it occurs. This is particularly necessary because one standard method for lead estimation has, as a preliminary step, the evaporation of 500 ml. of water to dryness and the ignition of the residue to remove organic matter.

There can be no question that the water supplies in this practice have in the past dissolved lead from piping in amount exceeding the W.H.O. standard limit, and sometimes very considerably above this. It should be noted however that 43% of the water samples taken were below this limit (see table 2). A relatively mild transitory illness was associated with evidence of increased lead absorption by

all the range of tests available - punctate basophilia, increased urine coproporphyrin and increased blood lead content. Such evidence was not present on every occasion however and the tests would not discriminate between recent absorption and mobilisation of previously stored lead. Complete proof of lead as the cause is therefore lacking.

More severe illnesses were noted in houses where the water supplies were found to contain most lead and this especially applies to the two dogs on a very bad supply. From symptoms, blood lead and brain lead estimations, these suffered from lead encephalopathy, but the peculiar distribution of lead in their tissues poses a very considerable problem. Where the lead content of the water may rise to 0.90 p.p.m. it seems unreasonable to suggest that the lead poisoning derived from some other undetected source. On the other hand it is disturbing to postulate that lead compounds in that water supply showed the affinity for neurological tissue which has until now been associated only with the organic lead compounds used in the petroleum industry.

In these studies laboratory methods of investigation have often shown up in a poor light. We lack a sensitive specific test for the earliest deviation from physiological normality for man, woman, child and unborn foetus which can easily be applied and can give rapid results in areas where laboratory services are poorest. The coproporphyrin test, despite its lack of specificity, is considerably more sensitive than the punctate basophil test which was formerly most widely used. If the pink fluorescence is, as it is claimed, the indication of an early toxic effect on haemoglobin formation then its presence in a maternity case also indicates the possibility of toxic effects on the foetus. In view of this, the standards required must be much more stringent than those which are accepted in industry from which the maternity patient is so carefully excluded.

The disastrous effects of Thalidomide in early pregnancy have brought into prominence the question of toxic effects on the foetus. In the present climate of public and professional opinion any positive reaction, however slight, in a test for toxic effects in pregnancy, is unacceptable. If maternity patients show features which can reasonably be described as deviations from the normal physiology of pregnancy then some action is necessary.

The maternity patients in this community have shown levels of urine coproporphyrin excretion which are different from those prevailing in the city of Edinburgh and these levels were able to be modified by treatment which would be expected to reduce lead absorption. This in itself is sufficient to justify the suggestion that alteration is required in the lead content of their food and drink so that measures to interfere with lead absorption are rendered unnecessary.

From the evidence which has been presented it can be claimed that harm has been demonstrated to occur from the absorption of lead in the community studied. Where a whole community is involved the situation is very different from that pertaining in lead using industries where men can be supervised and suspended from contact with lead if they show early signs of toxic effects.

Summary.

It is necessary to summarise briefly some of the observations which have been made in these studies before attempting to draw conclusions.

It was stated clearly in Roman times that drinking water should not be supplied through lead pipes because of the harmful effects of certain lead compounds, but this has not been heeded.

An authoritative opinion in Britain in 1934 was that all water delivered through lead pipes might be expected to contain lead but the amounts in many cases might be so minute as to be of no practical significance. The World Health Organisation in 1963 established an International Standard limit for the lead content of drinking water of 0.05 p.p.m. but there is no full acceptance of this by British water authorities and there is no legal standard for the limit of the lead content of water in this country. It has been noted with concern that one method used for water analysis is over a hundred years old and has not sufficient sensitivity for this recent International Standard. Analysis of water samples from the area of these studies has on a large number of occasions yielded results above 0.1 p.p.m. Analysis of a specimen diet revealed that it had a lead content at a level described by an American authority as the limit of safety and left no margin for any addition to the lead intake from drinking water.

When screening tests for increased lead absorption were applied to large groups of the population by two established industrial methods (punctate basophil counts and urine coproporphyrin estimations) it was found that a majority of the patients giving abnormal results had symptoms of gastro-intestinal disturbance. No bacterial or virus cause could be found for symptoms of this kind but some such patients had a

definite increase in blood lead level and this was also found in four dogs studied. The maternity patients in this practice showed a different pattern of urine coproporphyrin excretion from that prevailing in a hospital ante-natal clinic in Edinburgh. This difference was modified by treatment which was designed to reduce the absorption of lead.

A small group of men exposed to a well recognised industrial hazard from lead were found to be inadequately covered by the regulations made under the Factories Acts.

Conclusions.

From these studies it is possible to draw conclusions of two different types. The first relate to general practice observations and other field studies and the second to matters requiring official regulation or further laboratory investigation.

(A).

1. In areas where gastro-enteritis recurs frequently and no bacterial or virus cause can be found, consideration should be given to the possibility of this being of chemical origin. If the water supplies are soft with a pH less than 7.8, they should receive special attention.

2. Where plumbo-solvency has been demonstrated exceeding the World Health Organisation International Standard limit of 0.05 p.p.m., the maternity patients should be first to be studied. Their sensitivity to the toxic effects of lead is well recognised, and the industrial screening methods of urine coproporphyrin estimation and punctate basophil count can easily be added to the routine of ante-natal care. Temporary remedial measures can even be applied to these patients without causing widespread local disquiet, if these are found necessary before the water supplies to the community as a whole have been improved.

3. In studies of maternity patients on plumbo-solvent water supplies in the future, attention should be paid to any alteration in the incidence of Pre-Eclamptic toxaemia and to the nature of any congenital anomalies, to see whether the observations made on a small group of maternity patients in Innerleithen are repeated elsewhere.

(B)

1. There is no reason to dispute the W.H.O. International Standard limit of 0.05 p.p.m. for the lead content of drinking water or the comments of Cox (1964) that toxic effects occur above this level. This should be adopted as a legal standard in Britain but ample warning should be given so that water undertakings can have time to make the necessary alterations. Such a legal standard should cover the supply of water to any tenant. Existing legislation gives power of inspection and sampling.

2. Analysts should be requested to state the method used and the sensitivity thereof when giving negative reports on toxic substances such as lead, in water supplies.

3. Regulations are urgently required to provide medical and haematological or biochemical examination for all men using oxyacetylene apparatus to cut lead painted metal surfaces, and to bring them within the terms of the Factories Acts.

4. Further studies are required on the nature of chemical compounds of metals which may be found in domestic water supplies, on their local effects on the gastro-intestinal tract, and on their absorption.

Acknowledgements.

These studies have been made possible by a grant for medical research from the Secretary of State for Scotland for the period from July 1961 to July 1964.

I am deeply indebted to Dr. W. McNaught and the staff of the Border Hospitals Group Laboratory and to Mr. J.I. Waddington and the staff of the laboratory of the Tweed River Purification Board for the great amount of work which they have undertaken on my behalf.

I have found it necessary to seek the advice of a large number of experts in different subjects and have been greatly helped by their guidance, encouragement and assistance.

I am particularly grateful to Professor R.E. Lane of the Nuffield Department of Occupational Health, University of Manchester, for recommending the Donath apparatus as a suitable instrument for a general practitioner to use in his consulting room, and to Mr. E. King of that department for advice and for estimations of the lead content of a complete two day diet.

The Royal (Dick) Veterinary College has provided clinical, laboratory, and post mortem examinations of dogs and my thanks are due in particular to Dr. Barden and Dr. Pavor for blood and tissue lead analyses and estimations of the lead content of milk.

I am also indebted for milk analyses to Dr. R. Allcroft of the Ministry of Agriculture Central Veterinary Laboratory, Weybridge, Surrey.

Dr. A. Goldberg of the Western Infirmary, Glasgow, very kindly provided facilities for blood and urine lead estimations after the one year research grant for this purpose to Dr. McNaught from the Border Hospitals Board of Management had expired.

I am very grateful to Dr. S.L. Tompsett of the Northern General Hospital for lead analyses of the tissues

of two patients whose post mortem examinations were done in Edinburgh and for all other lead analyses.

My thanks are also due to Dr. D. Purves, Edinburgh School of Agriculture, for soil analyses, to Dr. R.E. Kressman, (Permutit Co. Ltd.) for information and experiments on salts of humic and fulvic acids, to Drs. Powell, Spears and Jones of Sunbury on Thames for the analyses detailed on pages 80 and 82, and to Dr. E.D. Hughes, (J. Lyons & Co. Ltd., London), for the confirmatory analysis in Table 7, page 74.

Professor S.C. Frazer of the Department of Chemical Pathology, Aberdeen, has given advice on the Donath apparatus and has provided Table 24 on page 129 for which I am very grateful.

Mr. J.M. Ragg, Macaulay Institute for Soil Research, Aberdeen, has very kindly supplied a simplified soil map of the practice area (Figure 1. page 32).

Urine specimens from hospital patients for various studies of coproporphyrin excretion have been obtained by the kind permission of Professor R.J. Kellar, Dr. J.M. Murdoch, and Dr. Maxwell Jones.

I am indebted to those colleagues in general practice who have supplied urine samples and provided access to cases: Dr. I.R. Henderson, Dr. R.B. Wilson, Dr. G.M. Third, Dr. B.J. Brown and Dr. G.M. Gill.

Dr. E.M. Desmit of Utrecht has obtained colorimeter discs for the Donath apparatus for me and has also supplied translations of Dutch publications and provided Plate 3.

Advice on the legal aspects of industrial plumbism was kindly given by Dr. A.T. Doig and Mr. J.N. Cartwright of H.M. Factory Inspectorate, and on statistics by Mr. S.A. Sklaroff of the Usher Institute of Public Health.

The librarians of Edinburgh University Central Medical Library and the Royal College of Physicians, and the College of General Practitioners Photocopying Service have been most helpful.

I am grateful to the Medical Photography Unit of Edinburgh University for photographs of x-ray plates (pages 201-3) and for mounting my photographs.

My two successive secretaries Mrs. I. Donaldson and Mrs. A. McQueen have played a part in the compilation of this thesis which has been quite invaluable.

Part of these studies has been included in papers read to the Medico-Chirurgical Society of Edinburgh (February 1963), at a College of General Practitioners Symposium on Research in General Practice (September 1963), and to the Section of General Practice of the Royal Society of Medicine (December 1963). A dissertation on observations on Maternity Patients was awarded the Sir Charles Hastings Prize of the British Medical Association in 1963.

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